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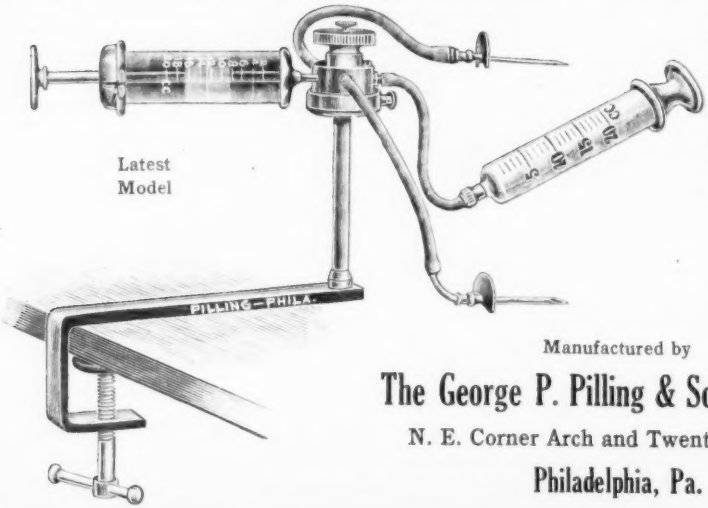

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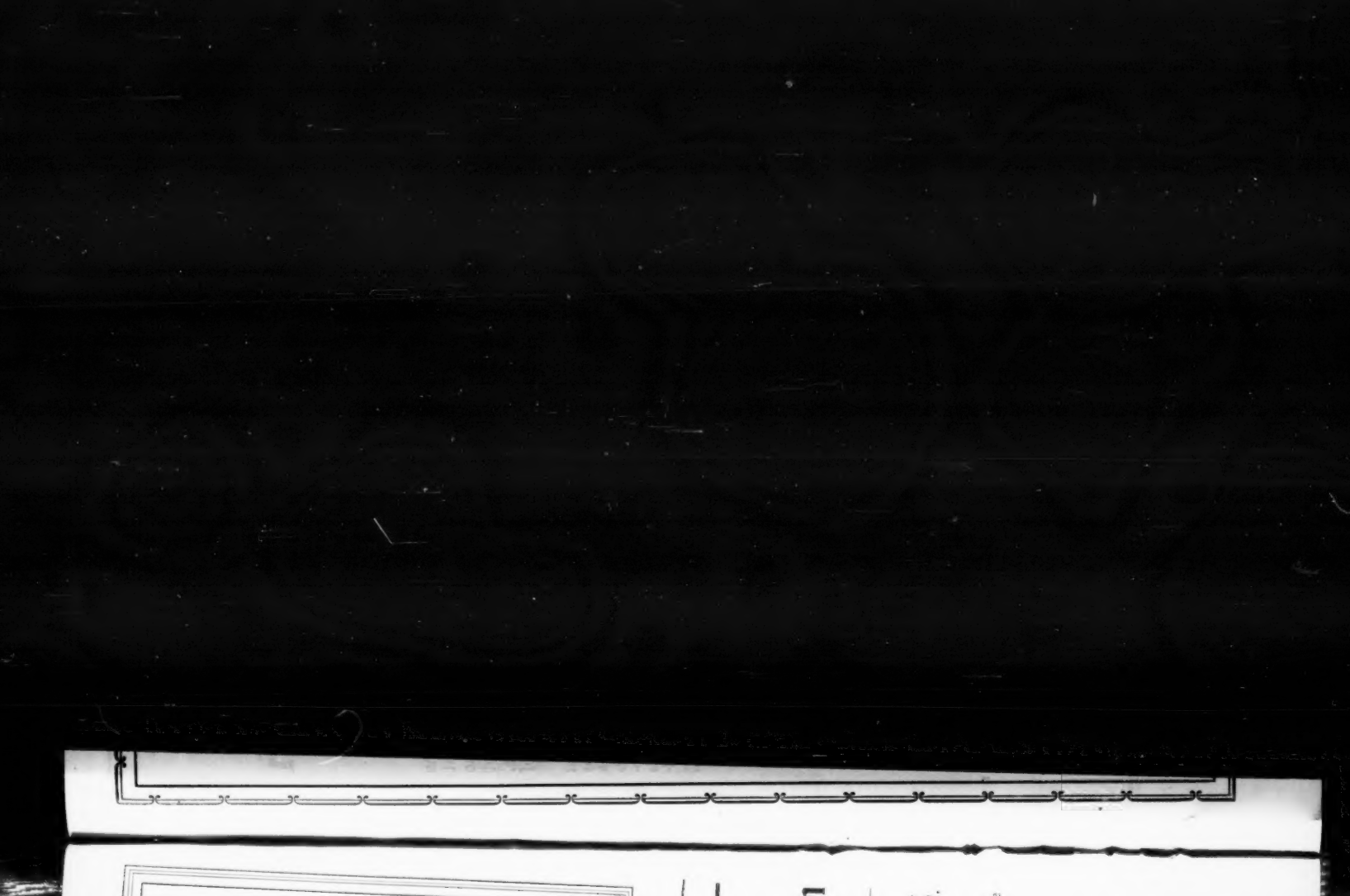

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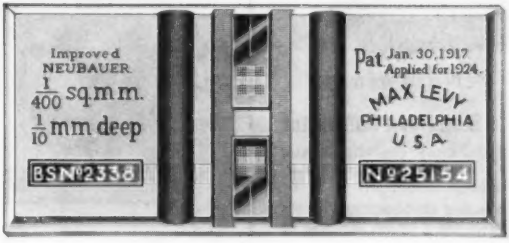

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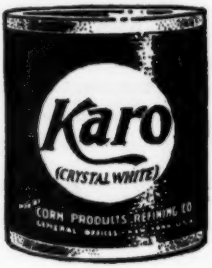

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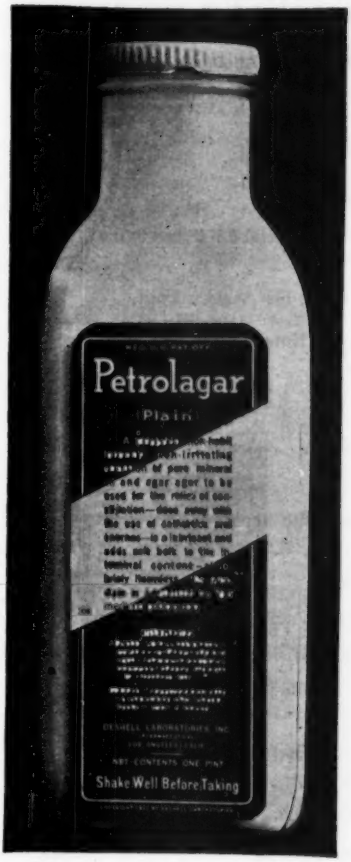

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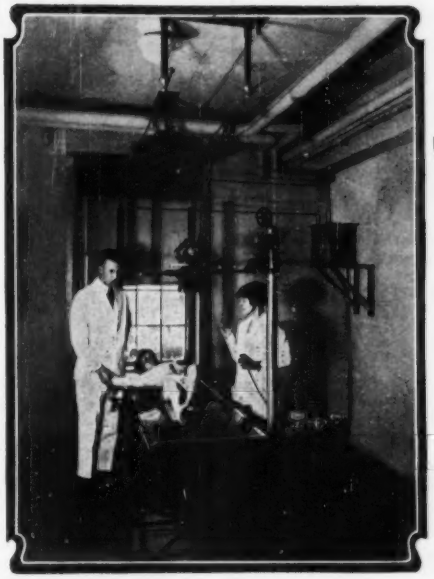

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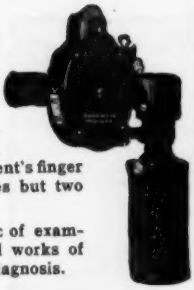

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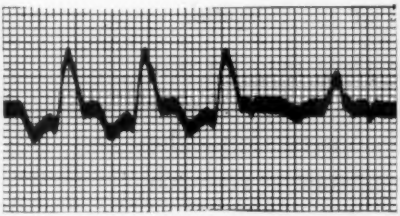

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OF THE MEDICAL SCIENCES

OCTOBER, 1924

ORIGINAL ARTICLES.

INFECTION OF THE GALL-BLADDER IN RELATION TO PERNICIOUS ANEMIA

By Noble Wiley Jones, M.D.

AND

Thomas M. Joyce, M.D.,

PORTLAND, OREGON.

(From the Departments of Medicine, Surgery and Pathology of the University of Oregon Medical School.)

Six years ago, one of us (N. W. J.) began the study of the case of Mrs. G. (Case I) who gave a history of weakness and anemia that had existed in a periodically relapsing manner for seven years and was punctuated by occasional attacks of rather severe pain in the right upper abdomen. She presented a lemon-tinted skin, a moderate degree of glossitis and a blood picture possessing the so-called persistent characteristics of a pernicious anemia during the period between relapses; namely, a plus color index, irregular and large red blood cells with irregular staining properties but without nucleated red cells. She was studied for a month in hospital as a borderline anemia, that is, a probable pernicious anemia which at the time does not show the presence of megaloblastic cells, and because of the continued pain and soreness in the upper abdomen she was operated for chronic gall-bladder disease. This condition was found and the gall-bladder was removed. A hemolytic streptococcus was obtained in pure culture from it. During convalescence the lemon tint of the skin disappeared and the blood assumed, in the course of a few weeks, the picture of a mild grade of secondary anemia. The patient is a true general asthenic in build and state

of health; she has never been robust; is not strong now, but through two severe protracted illnesses during the past six years she has retained a general asthenic type of health and has not reverted to the picture of pernicious anemia.

The outcome of the treatment in this case suggested to the observer at the time as possibly of interest in throwing some light upon the hidden cause of Addison's idiopathic anemia, and since then all similar cases have been studied with this in mind. But the diagnosis of chronic cholecystitis could not be made with sufficient positiveness in other patients to justify exploratory operation, so that for several years there was no opportunity to study the question further. With the development of the newer technic of George and Leonard for the roentgenological study of the gall-bladder, however, the problem was taken up again. During the past year and a half several cases of borderline anemia and of frank pernicious anemia have been intensively studied from this standpoint. To our associate in roentgenology, Dr. Dorwin Palmer, we owe very much for the clinical recognition of existing gall-bladder disease in these patients. Operation on 2 of the patients depended wholly upon the roentgen-ray evidence. The gall-bladder in 1 instance appeared macroscopically normal but was removed because of the positive shadows obtained on the films and because of the anemia. The results of this study are now detailed.

A cursory review of the prominent points in the history of pernicious anemia is sufficient to impress one with the probability that the anemia, which bears this name, is a symptom-complex rather than a disease entity and that various hemolyzing agents may produce the picture if they have the opportunity to work within the body in a slow manner over a long period of time. In fact, clinical observation of any series of cases suggests the same thought, for the downward course is a very variable one. It may be rapid, comparatively speaking, without remissions and lasting only a few months; it may present the ordinary frank pernicious anemia course which continues two or three years and is characterized by several remissions and relapses in the meantime; and then again it may present the borderline picture which may continue for years and is a pernicious anemia in all appearances save that of not having megaloblastic cells in the circulation. This variable clinical picture was noted by Addison[1] in 1855 and more in detail by Biermer[2] in 1872. William Hunter has maintained since 1890 that oral sepsis constitutes the source of the hemolyzing agent and that the tongue and the stomach and intestinal mucosa become infected secondarily. In a British Medical Association Lecture in 1921, Hunter[3] makes the statement that the tongue in true pernicious anemia has become by reason of the oral sepsis the actual focal site for the infection which causes the disease and suggests the name of "glossitic anemia" for it. He does not offer evidence substantiating this belief.

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The first important contribution to the etiology of a pernicious type of anemia was that of Schaumann and Tallqvist[4] (1898) who found a hemolytic substance in the head and body of the fishworm, Bothriocephalus latus, and proved that it was the cause of the pernicious type of anemia in persons infected with this parasite. Schaumann[5] had already (1894) reported a study of 72 cases of fishworm anemia and had found the same clinical picture and the same megaloblastic metamorphosis of the bone-marrow as seen in true Addisonian anemia. The red blood cells averaged 131,100 per cm. in men and 1,272,000 per cm. in women. The bloods of all the patients showed megaloblasts in the circulation. Most of them had chronic achylia gastrica. The same changes were produced in dogs by feeding them extracts of the worms. Faust and Tallqvist[6] determined that this hemolytic substance is oleic acid and that it owes its hemolyzing property to the fact that it is an unsaturated fatty acid.

The clinical picture and the morbid anatomy of uncinariasis anemia may be identical with that of true pernicious anemia (Ashford and King[7]). The hemoglobin content has been as low as 8 per cent (Dare and v. Fleischl) and the red blood cell count as low as 754,000 per cm. These extreme instances are associated with megaloblasts and the other characteristics of pernicious anemia. Eosinophila is variable. The more severe the intoxication the fewer the eosinophiles; they may be absent. These authors state that eosinophila shows a corresponding degree of resistance to the toxin. The bone-marrow may also show the same gray-red appearance and the same changes microscopically as in pernicious anemia, but usually also numerous eosinophilic myelocytes and myeloplaxes are present. Whipple[8] quotes Preti as having found a hemolytic substance in Old World hookworms, which the latter believes to be related to the lipoids and to be similar to the hemolysin of Bothriocephalus latus found by Faust and Tallqvist. Whipple[9] has found a weak non-specific hemolysin in New World hookworm which is soluble in salt solution, is destroyed by heat, and may be obtained in concentrated extracts from the bodies of the worms. The hemolysin acts on human blood and on that of laboratory animals. Whipple does not believe, however, that this weak hemolysin has much to do with the anemia of uncinariasis but that it is produced in the main by the direct extraction of blood from the bowel wall by the parasites, inasmuch as whole and partly disintegrated red blood cells floating in a bloody fluid are passed out from the intestinal tracts of the worms. From the work on experimental anemia of Bunting, who found that he was unable to produce a megaloblastic anemia by means of repeated hemorrhages alone, one would be inclined to believe that the hemolysin of the hookworm must play a role in the megaloblastic picture found at times in man.

Bunting's[9] work (1905–1907) on experimental anemia is instructive. He produced what seemed like true pernicious anemia in rabbits and dogs by repeated small intravenous injections of ricin and of saponin. He was unable to produce such a type by repeated small hemorrhages, which caused a secondary type with an occasional normoblast in the blood-stream, the bone-marrow never showing evidence of injury. In producing a pernicious type of anemia by means of hemolytic agents, it was necessary to place them into the circulation in sufficiently large quantities to saturate the red cells in the blood-stream and to exert a direct harmful influence on the erythrogenetic centers of the bone-marrow, which alone leads to a megaloblastic metamorphosis. He concludes (*a*) that a secondary anemia due to a toxin, as for instance, that of tuberculosis, is found when the toxin is taken up by the red cells and the bone-marrow is left free to regenerate; and (*b*) that a pernicious type of anemia is found when the toxin injures the erythrogenetic centers in varying degree and prevents a normal regeneration. An imperfect and often a short-cut regeneration leads to the formation of immature and megaloblastic cells, both of which may then be found in the marrow and in the blood-stream. It is produced only when the toxin is introduced in sufficiently large quantities. Thus a severe secondary anemia may assume a pernicious type. The red cell crises then are expressions of severe injury to the bone-marrow rather than of regeneration. Thus, Bunting believes that true pernicious anemia is due to some primary hemolyzing agent circulating in the blood and affecting the bone-marrow secondarily. The marrow change is not the primary lesion. He believes both Bothriocephalus latus anemia and experimentally produced anemias seem to prove this statement.

Madler[10] (1913) produced crises of pernicious anemia in rabbits by feeding them large quantities of olive and cotton-seed oil. He believes that the toxicity depends on the amount of unsaturated fatty acids and that the anemia is produced in the peripheral circulation by its direct attack on the red cells. The effect on the bone-marrow he believes to be due to the excessive demand placed on it. One may easily believe, however, that, if the hemolyzing agent of Bothriocephalus latus is oleic acid, an unsaturated fatty acid, and if the toxic substance of olive or cotton-seed oil is the same, the action of the hemolysin on the bone-marrow centers may be direct, as Bunting maintains, if there is a sufficient quantity present in the circulation.

The hemolytic action of the spleen as a causative agent in pernicious anemia need be mentioned only in passing. Eppinger[11] and v. Decastello[12] brought forth this opinion independently in 1913. It led to splenectomy in a number of persons with pernicious anemia. One of us (N. W. J.) studied 7 such patients before and after operation without seeing any material change from the

ordinary variable clinical course. The procedure has now been abandoned.

Association of pernicious anemia and chronic gall-bladder disease has been noted in medical literature from time to time. Probably Georgi[13] (1887) was the first to mention it in a rather detailed report of a case presenting a frank pernicious anemia, gall stones being found at autopsy. This report called forth at once a retort from Ewald[14] who cited the autopsy of another patient dead of pernicious anemia, in whom no macroscopical evidence of gall-bladder disease was found. Percy[15] (1916) reported 37 cases of pernicious anemia operated upon for the removal of the spleen. The gall-bladder was removed twenty times for chronic cholecystitis and the appendix seventeen times because of chronic inflammation. In 9 cases the spleen, gall-bladder and appendix were studied bacteriologically. Hemolytic streptococcus was obtained seven times from some of these tissues, the Streptococcus viridans four times and the Staphylococcus albus once. The colon bacillus was also found in 5. Percy states that 58 per cent of 24 cases "were clinically in good condition" at varying intervals of time. One at the end of two years and eight months "is clinically perfectly well and carries no evidence of pernicious anemia in her blood, except that an occasional normoblast can be found." Later reports from this series of cases have not been obtained. Splenectomy was performed as the primary feature of the treatment, and removal of the gall-bladder and appendix was done as a part of the general process of ridding the body of septic foci, along with septic teeth and tonsils Giffin and Bowler[16] (1923) in a review of 628 cases state that 108 cases were associated with other diseases and that of this number 10 had had the clinical diagnosis of gall-bladder disease in addition to that of pernicious anemia. None of these patients came to operation. They state "On clinical examination no very convincing evidence of the condition (gall-bladder disease) is found."

This brief summary of the history of what is known regarding the etiology of pernicious anemia leads us now to recounting the following case records. Analysis of the important points in them will be discussed later. The pathological studies have been made by W. C. Hunter of the Department of Pathology with the counsel and aid of Dr. Benson, head of the department.

Case Reports. CASE I. Mrs. G., aged forty-five years, five para, three children living, was first seen June 6, 1917, complaining of general weakness, exhaustion, loss of weight and irregularly recurring attacks of pain and soreness in the upper abdomen, associated with constipation or, at times, bowel looseness. She had never been strong, but seven years ago she suffered a postpartum hemorrhage, since which time she has had a pale skin. At first it was a white

paleness; some years later it became lemon tinted, a color noticed by herself and her family. There were periods when she had numbness of the extremities. She had had measles, scarlet fever and sore throat earlier in life. At twenty all of her teeth were extracted, presumably for sepsis. Her family history was negative.

Examination. The patient is of a slight, asthenic build, moderately lemon-tinted skin, no jaundice. There is a moderate glossitis, a hemic heart murmur and some epigastric tenderness. The stomach acidity is 20 to 32; well chymefied food, and no blood. The stools show some blood from small hemorrhoids; no parasites. Five blood examinations, while in hospital from June 27 to July 17, gave practically the same findings; hemoglobin 80 to 85 per cent; red blood cells 3,680,000; white blood cells 7000; differential count: polymorphonuclears 65 per cent; small mononuclears 33 per cent; large mononuclears 4 per cent; transitionals 2 per cent; nucleated red blood cells negative; anisocytosis, poikilocytosis and polychromatophilia present; Wassermann negative.

Treatment. The patient was treated as a borderline anemia case, *i. e.*, a pernicious anemia which did not show nucleated red blood cells in the circulation. Receiving no relief from abdominal distress, she was operated upon July 20, on the assumption that she had a chronic gall-bladder disease. A large, distended, chronically infected gall-bladder was removed. The bile was greenish in color and contained much sediment. A hemolytic streptococcus was obtained from the gall-bladder wall. The appendix showed a moderate degree of obliterative inflammation.

Course. During the succeeding few weeks the patient improved slowly, as the general asthenic always does; her skin became clear and more or less pink in color. August 27, hemoglobin was 90 per cent; red blood cells 4,100,000; white blood cells 7100 with normal differential count. Irregular red blood cells and poikilocytes were present but polychromatophilic staining not. No nucleated red blood cells had been seen in six examinations. May 11, 1918, blood examination was recorded as follows: Hemoglobin 85 per cent; red blood cells 5,250,000; white blood cells 6300 of normal differential count. A few irregular red blood cells were seen but no irregular staining. In 1921, the patient suffered a supposed influenzal infection and some form of epidemic jaundice; at least, other members of the family and of the community had similar attacks of jaundice. As a result of this infection she was ill and weak for several months. May 3, 1921, blood examination showed hemoglobin 80 per cent; normal red cells 4,000,000; white blood cells, 9650. In 1922 the patient was ill, in and out of bed, with a sinus infection for nine months. On March 21, 1923, three blood examinations gave hemoglobin 80 per cent; red blood cells 4,500,000; white blood cells 6450 with normal differential count. There were some slightly irregular red blood cells but the general appearance of the blood

was that of a mild secondary anemia. The patient, herself, felt quite well, weighed 125 pounds, the skin was clear and the tongue showed no particular evidence of inflammation or atrophy.

Comment. The symptoms and physical findings in this case were those of a so-called chronic borderline anemia; an anemia characterized by the presence of the toxic or inflammatory symptoms of pernicious anemia and a blood picture possessing the permanent characters of pernicious anemia blood; namely, a plus color index and irregular shapes, sizes and staining properties of the red blood cells, but showing no nucleated red blood cells in the circulation. In addition to this, certain symptoms permitted the diagnosis of gall-bladder disease. The gall-bladder was removed and a hemolyzing streptococcus was obtained in pure culture from the wall. Six years have elapsed since the operation. The patient is fairly well. She has not progressed as a case of true pernicious anemia and the blood picture has regained fairly normal characteristics.

CASE II.—C., aged fifty years, was first seen February 7, 1916. For two years he had suffered spells of weakness, paleness, numbness and burning of the hands and feet, muscle soreness, constipation and distress in the abdomen and a mucous discharge from the nose. During the intermissions he has regained moderate health.

Examination. Heavy, gaunt type of build, pale, lemon-tinted skin and mucous membranes; no icterus; former dental sepsis; hyperplastic ethmoiditis with obstructing septal deflection. Stomach analysis shows complete achylia. The stools contain neither blood nor parasites. During February and March, 1916, while under treatment for pernicious anemia, the blood showed hemoglobin 73 to 90 per cent; erythrocytes, 2,420,000 to 3,480,000; leukocytes, 9000 to 4350; polymorphonuclears, 80 to 65 per cent; small mononuclears, 16 to 24 per cent; large mononuclears, 1.5 to 7 per cent; transitionals, 1 to 3 per cent; basophiles, 0.5 to 1 per cent; myelocytes, 1 to 1 per cent; normoblasts 2 cells found, megaloblasts negative; anisocytosis, poikilocytosis and polychromatophilia present. September 20, 1916, the hemoglobin was 100 per cent; erythrocytes, 5,280,000; leukocytes, 8600; 1 normoblast, fewer macrocytes and less irregular staining of the red cells was noted than formerly. In 1917, the patient spent four months in Johns Hopkins Hospital under treatment for pernicious anemia. September, 1921, four blood examinations showed hemoglobin 90 to 95 per cent; erythrocytes, 4,264,000 to 5,000,000; leukocytes, 6800; no nucleated red cells, moderate polychromatophilia and some macrocytes. July 19, 1922 to August 29, 1922, while under treatment, the hemoglobin was 60 to 82 per cent; erythrocytes, 1,240,000 to 3,370,000; leukocytes, 3200 to 6400. There were no nucleated red cells but marked variation in size and staining was present.

Positive roentgen-ray shadows of the gall-bladder were obtained July 19, and August 31.

Treatment. The patient was treated four times in hospital for pernicious anemia during these six years. Cholecystectomy and appendectomy were made September 7, 1922 (by T. M. J.).

Pathological Report. The wall of the gall-bladder is slightly atrophied. The mucosa is bile-stained and appears atrophic. Sections disclose a thinning and scarring of the wall and atrophy of the mucosa. Sections stained for bacteria reveal the presence of a few groups of organisms looking like staphylococci. A few diplococci are also present.

Pathological Diagnosis. Chronic atrophic cholecystitis.

Course. Convalescence from the operation was prompt. The lemon-tinted color of the skin cleared quite rapidly, the nail beds and mucous membranes showing pink. Fourteen blood examinations during the month in hospital showed a fairly graduated transition from the pernicious picture to a moderate secondary anemia. The last one, October 11, 1922, showed hemoglobin, 90 per cent; erythrocytes, 4,300,000; leukocytes, 8100; polymorphonuclears, 61 per cent; small mononuclears, 32 per cent; large mononuclears, 4 per cent; transitionals, 1 per cent; eosinophiles, 2 per cent; nucleated red cells, negative; very slight changes in the character of the red cells.

A month after operation the numbness and hurting of the legs and arms and at times over the entire body became worse. Since Christmas these symptoms have slowly abated and do not bother the patient as much now. He has returned to his work as a timber bruiser but is not yet strong enough to stand hard work. He feels, however, that he is gaining in strength progressively. Examination on May 5, 1923, revealed a physical state quite different from that seen at any time during the past seven years. The patient's color is good; the skin is red from his out-of-door life, and there is no evidence of sallowness or lemon tinting. The tongue shows a moderate glossitis but is not sore. The knee kicks are absent. There is slight swaying of the body with the eyes closed but no distinct incoördination. The patient states that a certain unsteadiness at night is less now than it formerly was. Four blood counts show hemoglobin, 88 per cent; erythrocytes, 4,570,000; leukocytes, 5200; with normal differential count. The red blood cells are well stained. There are a few macrocytes, and in the four examinations 1 normoblast is found. Undoubtedly the blood still possesses slight evidence of its former pernicious type but it approaches more nearly the picture of normal blood than it has done since the patient was first seen in 1916. His general health and strength is also better.

Comment. This patient had suffered for about eight years with the symptoms of a slowly progressing frank pernicious anemia

before the diseased gall-bladder was recognized and removed. A certain degree of change had taken place in the spinal cord as evidenced by the severe paresthesiæ, the loss of deep reflexes and a slight Rombergism. Since the operation the patient has regained much of his former health and the cord symptoms seem to be lessening. How much permanent damage has been suffered by the spinal cord and the erythrogenetic centers of the bone-marrow only time will tell. Cultures from the gall-bladder were not obtained. Microorganisms possessing the morphological characters of a staphylococcus and a diplococcus were found, however, in stained sections of the gall-bladder wall. Nine months have elapsed since the patient was operated upon and he seems to be progressively moving away from the picture of pernicious anemia rather than downward as seemed to be the one prospect in the summer of 1922.

CASE III.—Mrs. K., aged twenty-nine years, 4 para, was received January 29, 1923. She had suffered from recurring periods of weakness, paleness, nausea and constipation since scarlet fever at twenty years of age. Her skin had been of a sallow type of paleness since this time, but following a miscarriage in June, 1922, it has become a more pronounced lemon tint and the weakness and distress more severe. She has suffered slight paresthesiæ. Her history revealed typhoid fever at eighteen, measles in childhood, scarlet fever at twenty, influenza at twenty-six, two miscarriages and a phlebitis of the right leg.

Examination. Extreme asthenic type of build, weight 116 pounds, skin lemon tint and pale, severe dental sepsis; the tongue shows a blotchy glossitis; the stomach complete achylia; the gall-bladder gives faintly positive shadows on the films, and there is no indirect roentgen-ray evidence of gall-bladder disease. The stools are negative for blood and parasites. Nine blood examinations during a month in hospital showed, on an average, hemoglobin, 80 per cent; erythrocytes, 3,990,000; leukocytes, 12,000 to 6800; no nucleated red cells, anisocytosis, poikilocytosis and polychromatophilia present. The extraction of all teeth did not change the blood picture. Blood Wassermann was negative.

Treatment. After one month in hospital with bed rest, arsenic, hydrochloric acid, and so on, the patient was operated upon March 5, 1923 (by T. M. J.). The gall-bladder did not reveal any gross appearance of disease. The lymph nodes along the common bile duct were not enlarged. The common bile duct, itself, seemed to be somewhat dilated. In spite of the normal appearance and because of (*a*) the positive roentgenological evidence and (*b*) the type of the patient's anemia, the gall-bladder was removed. The appendix showed more evidence of disease and was also removed.

Pathological Report. The gall-bladder wall is slightly thickened and fibrous. The mucosa is bile-stained and atrophic. Sections

disclose a desquamation of the epithelium of the mucosa; slight diffuse fibrous increase in the muscular coats and the rest of the wall. In the sections stained for presence of bacteria a few micro-organisms resembling staphylococci are found. Cultures of the wall of the gall-bladder yield a slightly hemolytic Staphylococcus albus. Cultures of the bile are negative.

Pathological Diagnosis. Slight catarrhal cholecystitis.

Course. The patient convalesced quite rapidly from the operation; within one week the lemon tint of the skin was fading rapidly. On March 27, 1923, the blood showed hemoglobin, 89 per cent; erythrocytes, 4,700,000; leukocytes, 6000; polymorphonuclears, 69 per cent; small mononuclears, 24 per cent; large mononuclears, 4 per cent; eosinophiles, 1 per cent; basophiles, 1 per cent; transitionals, 1 per cent; nucleated red cells, negative; poikilocytes few, macrocytes negative, polychromatophilia absent.

May 5, 1923, the patient was again examined. She states that she feels stronger and has a desire to work for the first time since she became ill. Numbness in both hands lasted for a week after she went home but has not returned. The skin is now pale pink in color; it has lost its lemon tint. The septic tonsils still remain; they are to be removed later. The blood shows in four counts—hemoglobin, 75 per cent; erythrocytes, 4,540,000; leukocytes, 7000; of normal differential count. The red cells stain uniformly with pale centers. There are no macrocytes and no nucleated red blood cells are seen. The picture is that of a moderate grade of secondary anemia.

Comment. The transformation of this patient's blood picture after cholecystectomy from a pernicious type to that of a secondary anemia was quite rapid. A gain in general health has been quite as rapid also. From the gall-bladder wall Staphylococcus albus was obtained in pure culture and cocci resembling staphylococci were found also in stained sections. Although this patient is a general asthenic of marked degree, her progress toward recovery has seemingly been more rapid than that seen in Case II. It is possible that the pernicious anemia in this case has existed for only one year.

CASE IV.—H., aged sixty years, farmer, was received April 13, 1923. Paleness, weakness, shortness of breath and pains in the shoulders began one and a half years ago together with numbness in the ankles and knees, wrists and hands, and tingling of the toes and fingers. The patient has not lost much weight.

Examination. The skin is pale and lemon tinted. The mucous membranes are pale. The tongue is pale and glossy. The lower teeth and tonsils show infection. An upper plate is worn. The upper teeth were removed for sepsis. A hemic murmur is heard over the precordium. The stomach shows complete achylia. The

stools are negative. The antrum of the stomach is spastic. The bulb of the duodenum is drawn slightly to the right, and the lesser curvature margin is hazy. Films of the gall-bladder show positive shadows without stones. The blood Wassermann is negative.

Treatment. Ten blood examinations were made during four weeks in hospital under treatment. The first one showed: Hemoglobin, 40 per cent; erythrocytes, 1,780,000; leukocytes, 8850; polymorphonuclears, 35 per cent; large mononuclears, 6 per cent; transitionals, 1 per cent; eosinophiles, 1 per cent; normoblasts, 2; megaloblasts, 1. Many macrocytes and marked polychromatophilic staining was present. The last examination before operation showed: Hemoglobin, 71 per cent; erythrocytes, 2,450,000; leukocytes, 3600; 1 normoblast; polychromatophilia and anisocytosis were less marked than on entrance.

Cholecystectomy May 14, 1923 (by T. M. J.). Recovery from the operation was uneventful. The gall-bladder showed macroscopically little change from the normal. A small section of the liver was removed for examination. The change in the appearance of the patient during the first week was marked. The lemon tint of the skin disappeared quite completely and was replaced by a pink color. The blood showed: Hemoglobin, 76 per cent; erythrocytes, 3,080,000; leukocytes, 7200; polymorphonuclears, 72 per cent; small mononuclears, 14 per cent; large mononuclears, 9 per cent; eosinophiles, 4 per cent; transitionals, 1 per cent. The red cells stained fairly evenly and there were but few macrocytes.

Pathological Report. The gall-bladder is of average size, wall slightly thickened and scarred, mucosa intact, no concretions, contains about 15 cc of light brownish viscid bile.

The clipping from the liver measures 0.5 by 1 cm. and appears normal.

Microscopically there is a slight increase in the fibrous tissue throughout the wall of the gall-bladder. Scattered through the scar tissue are moderate numbers of small round cells. The mucosa is partially desquamated but the greater portion is intact and shows no noteworthy changes. Sections stained for bacteria disclose the presence of small numbers of organisms occurring in pairs and short chains.

Diagnosis. Slight chronic diffuse cholecystitis.

Bacteriological Findings. Cultures from the gall-bladder in meat infusion broth enriched with blood disclose the presence of non-hemolytic Staphylococcus albus. Whether this is a contamination from the skin of the patient or not is difficult to determine. No other microörganisms are found.

Bile. Sterile.

From the bit of liver tissue, alpha-hemolytic streptococcus, producing definite greenish zones about the colonies and occurring in both short and long chains, is isolated in pure culture.

Comment. The clinical appearance and the megaloblastic blood picture of this patient is typical of a true progressive pernicious anemia. The change in the general appearance of the patient, the rapid clearing of the skin and the equally rapid change in the condition of the red blood cells is seemingly more marked than that noted in the former three patients. The finding, however, of non-hemolytic organisms in the liver tissue and morphologically similar organisms in the wall of the gall-bladder brings up the question whether the anemia may be produced by the effect of some chemical substance entering the circulation from the infected gall-bladder rather than from the direct lytic action of the bacteria and their products on the red blood cells and the erythrogenetic centers of the bone-marrow. A similar organism was obtained at autopsy in Case VIII. A portion of liver tissue was cultured for the first time in this case. The organism obtained in pure culture bears resemblance to the morphological characteristics of that found in the stained sections from the gall-bladder wall.

CASE V.—Mrs. J., aged thirty-seven years, 2 para (1 miscarriage at three months, seven years ago) was received December 7, 1922. Patient complained of periodic weakness and paleness which began after a miscarriage seven years ago. For the last three years the spells have been especially severe, but during the summers she has partially regained health. She suffered from loss of weight and strength, shortness of breath, swelling of the feet, nausea, vomiting and constipation and numbness of the hands and feet.

Examination. There was found pale, lemon-tinted skin, dental plates (history of previous sepsis), moderate glossitis, hemic murmur over the precordium, edema of the legs, complete achylia and stools negative to blood and parasites. The urine, blood chemistry and blood Wassermann are negative. Positive shadows of the gall-bladder are obtained December 18.

Eight blood examinations from the 8th to the 29th, inclusive: December 8, the blood showed hemoglobin, 20 per cent; erythrocytes, 1,550,000; leukocytes, 5200; polymorphonuclears, 67 per cent; small mononuclears, 29 per cent; large mononuclears, 2 per cent; transitionals, 1 per cent; eosinophiles, 1 per cent; occasional normoblasts, no megaloblasts; anisocytosis, poikilocytosis and polychromatophilia was present. December 29, the blood count was hemoglobin, 10 per cent; erythrocytes, 440,000; leukocytes, 6600; polymorphonuclears, 59 per cent; small mononuclears, 40 per cent; large mononuclears, 1 per cent; normoblasts were present; megaloblasts 1, the changes in the red cells more pronounced than before.

The first megaloblast was found on December 22, 3 were found on the 26th, and 1 on the 29th. Death occurred December 29, 1922.

Autopsy. The body of a white female, aged thirty-seven years. There is a general pallor of the skin, teeth absent, gums smooth,

subcutaneous fat is light yellowish and finely lobulated. Lymph nodes in root of mesentery are hyperplastic. Mucosa of stomach pale and atrophied. Small hemorrhages are numerous beneath capsule of liver. Liver parenchyma is pale and friable and the blood which exudes is pale.

The gall-bladder is free from adhesions; its wall is slightly thickened and opaque. The bloodvessels beneath the serosa are unusually prominent. Bile is dark greenish-black and viscid. The mucosa is bile-stained but apparently intact. The biliary lymph nodes are slightly hyperplastic. Petechial hemorrhages are found in the serosa of the pancreas. Spleen is about one-third larger than normal, cut surfaces reddish, moderately firm and somewhat fibrous. Kidneys are pale and anemic. Heart is yellowish-brown and flabby, no valvular lesions. Lungs are unchanged. There is marked hyperplasia of the bone-marrow.

Microscopically. The muscle fibers of the heart are rather shrunken. A yellow pigment appears in most of the cells lying between the fibrils and especially around the nuclei. Some of the cells are vacuolated and appear to have contained fat droplets. There are no red blood cells in the vessels.

Gall-bladder. Sections disclose the mucosa to be bile-stained, denuded and roughened. There is a slight thickening in the submucosa. A lymphoid follicle is seen in one part of the serosa. In sections stained for bacteria a few cocci in short chains and a few diplococci are found.

Liver. The cord of liver cells stain palely and are quite shrunken so that the capillary spaces are relatively wide. Nearly all the cells but mostly those around the central veins contain fat droplets. There is much yellow pigment both intra- and extracellular. No bacteria are found in the sections.

Spleen. The Malpighian bodies are prominent. The pulp is packed with red blood cells and yellowish pigment, evidently from broken down red cells. The pulp is relatively free from lymphoid cells. The blood sinuses are definitely outlined but contain few red blood cells and many white cells.

Bone-marrow. Sections from a rib and the femur show marked cellular activity. The fatty reticulum present in the normal adult femur is replaced by active marrow elements so that the sections from the two bones are indistinguishable. The large number of megalocytes, megaloblasts and normoblasts seen among the marrow cells is striking. A differential count made of several areas to get an idea of the percentage of the different types shows approximately in each area, respectively: (*a*) 8 myelocytes, 10 myeloblasts, 5 normoblasts, 4 non-nucleated red blood cells; (*b*) 4 myeloblasts, 5 normoblasts, 4 non-nucleated red blood cells, and (*c*) 4 myeloblasts and myelocytes, 1 polymorphonuclear leukocyte and 4 lymphocytes.

Bacteriological. Cultures of the bile were negative for all organisms. B. coli was obtained from the gall-bladder wall, but this is thought to be a contamination.

Anatomical Diagnosis. Hyperplasia of the bone-marrow; generalized pallor of the skin; atrophy of gastric mucosa; multiple hemorrhages of serous membranes; chronic atrophic cholecystitis; pernicious anemia; hyperplasia of mesenteric and biliary lymph nodes; yellow atrophy and slight interstitial fibrosis and slight fatty changes of the myocardium.

CASE VI.—(Multnomah Hospital Service). W. H., aged twenty-three years, was received December 1, 1922. Patient had suffered for four years with relapsing weakness and paleness, swelling of feet, numbness of hands and feet, and periodic pain and swelling in left hypochrondrium for two years. During the past summer the patient was in bed for seven months with such an attack to which a chronic dysentery was added. The present attack of pain began one week before entrance to the hospital. It was associated with chills, fever and profuse sweating. He had developed an acute gonorrheal iritis from an old urethritis, smears showing Gram-negative intracellular diplococci. He presented a general septic appearance with a profound lemon-tinted type of anemia.

The history revealed measles and jaundice in childhood, left-sided pleurisy, many attacks of sore throat and a Neisserian infection three years ago.

Examination. A pale, asthenic male, profoundly weak, severe dental infection; first heart tone, left, possesses a rumbling murmur at times—absent at other times. There is diffuse abdominal tenderness, more marked in the left hypochrondrium, together with a mass felt beneath the left costal arch. The feet are edematous. The stomach chemistry is not investigated. The urine shows albumin and pus with Gram-negative diplococci and Gram-positive chained streptococci. Gall-bladder not examined. The blood Wassermann is negative and one blood culture is also negative. Six blood examinations showed hemoglobin, 68 to 58 per cent; erythrocytes, 2,944,000 to 1,896,000; leukocytes, 3000 to 4600; polymorphonuclears, 40 to 64 per cent; small mononuclears, 26 to 36 per cent; large mononuclears, 8.5 to 20 per cent; eosinophiles, 0 to 1.5 per cent; transitionals, 0 to 2.5 per cent; myelocytes, 2 to 4 per cent; nucleated red cells negative; marked changes in the size and staining of the red cells. Death, February 9, 1923.

Autopsy. This is the body of a moderately emaciated white man, aged twenty-three years, skin pale; skin about the ankles pits on pressure. Pelvis and abdominal cavities contain about 2 liters of straw-colored fluid. Liver is large. The lower pole of spleen is seen just below the costal margin in the left midclavicular line. Four septic anemic infarcts are present in the spleen. The upper

pole is adherent to the diaphragm by fibrous bands; when dissected away a well walled-off subdiaphragmatic abscess 2 x 3 x 5 cm. is found. The capsule of the spleen is tense. The cut surfaces disclose a moderate hyperplasia of the pulp and engorgement with blood. The spleen weighs 1500 gm. The gall-bladder is greatly swollen due to edema of the wall. Beneath the serosa there are numerous small hemorrhages. The sac contains viscid brownish bile. The biliary lymph nodes are hyperplastic. The main bile ducts are patent.

Each pleural cavity contains a liter of straw-colored fluid in which the lungs float. Petechial hemorrhages are abundant in the visceral pleural of each lung. The lung is densely adherent to the diaphragm. The pericardial sac is distended with straw-colored fluid. The heart is dilated and flabby; its musculature is pale. At the junctions of the leaflets of the mitral valve there is a ragged ulceration with destruction of a few of the chordæ tendineæ. The cut surfaces of the lungs reveal a passive hyperemia and atelectasis at the bases. The cut surfaces of the kidneys are dark, glomeruli red. In the liver the lobules are well outlined, parenchyma friable, and the blood which exudes is pale reddish and thin.

Microscopically the heart shows areas of focal necrosis, hyaline degeneration, and scar tissue, which has the appearance of having been recently formed, scattered throughout the myocardium.

Liver. Sections disclose a moderate atrophy of the cells, especially about the central veins, where also fatty changes and intra- and extracellular pigment is found. No bacteria in the liver. The abundance of pigment obscures the picture.

Gall-bladder. Sections reveal small hemorrhages in the serosa, marked edema of subserosa, moderate increase in fibrous connective tissue, and partial desquamation of epithelium of mucosa. A few round cells are present. Sections stained by Unna's alkaline methylene-blue method for bacteria disclose many organisms in chains that look like streptococci.

Spleen. The sinuses are filled with red blood cells and pigment containing phagocytes. There is a slight hyperplasia of the lymphoid cells. Other sections disclose septic anemic infarcts covered with fibrinous exudate.

Kidneys. There is hemorrhage, recent and old, into the subcapsular spaces of Bowman and into the convoluted and straight tubules.

Lungs. Chronic passive congestion and atelectasis.

Bone-marrow. Not examined.

Bacteriological. A pure culture of long-chained hemolytic streptococcus was obtained from the bile and the wall of the gall-bladder. Cultures from an infarct in the spleen gave the same organisms and B. coli. Cultures of the spleen pulp were negative. Intravenous injection of the organisms in a rabbit produced purulent arthritis

and bacteriemia in two days. The organisms were recovered from the joints and the heart blood. Cultures of the bile and gall-bladder of the animal were sterile.

Anatomical Diagnosis. Subacute ulcerative endocarditis—mitral valve; multiple septic infarcts in the spleen; small subdiaphragmatic abscess involving upper pole of spleen; focal necrosis and scarring of the myocardium; moderate atrophy; chronic and acute dilatation of all chambers of the heart; moderate ascites, bilateral hydrothorax, hydropericardium and edema of the ankles; chronic passive congestion of the liver; atrophy, fatty and pigment changes; chronic passive congestion of the lungs, atelectasis of lower lobe; subacute and chronic cholecystitis with hyperplasia of biliary lymph nodes; marked chronic anemia; moderate emaciation; chronic hyperplasia and hypertrophy of the spleen; petechial hemorrhages in visceral pleuræ and serosa of gall-bladder; hemorrhage in kidneys; fibrous pleuritis, base of left lung. Examination of bone-marrow was overlooked.

Case VII.—(Medical Division U. S. Veterans' Bureau). F. M., male, aged forty years, was not studied during life by us but came to autopsy by Dr. Hunter, March 9, 1923. The history from the Veterans' Bureau is that of a frank pernicious anemia beginning some time previous to January, 1918, and characterized by several relapses and remissions until death occurred March 8, 1923.

Examination. The patient is emaciated; weight 114 pounds; very anemic; of sallow, brownish hue; some dental and tonsil sepsis; hemic heart murmur. The blood on several occasions showed hemoglobin, 50 to 25 per cent; erythrocytes, 1,500,000; leukocytes, 3000. The red blood cells are irregular in shape, size and staining properties. There are no nucleated red blood cells found. A blood culture is negative.

Autopsy. This is the body of a poorly nourished white man, aged forty years. There is a general brownish pigmentation of the skin.

The gall-bladder is small, thick walled and contains a single large soft bile-pigment stone. The mucosa is desquamated and denuded. The cystic, hepatic and common bile ducts are patent. The surface of the liver is finely pebbled; the parenchyma cuts with increased resistance; the blood which exudes is pale and watery.

The lungs are emphysematous. On section, small discrete consolidations are seen. In the visceral pericardium are numerous petechial hemorrhages. The heart is large, flabby and pale. The musculature, especially at the bases of the papillary muscles, is pale and fatty. The endocardium presents the mottled appearance described as "tigering;" no valvular lesions. A number of calcified lymph nodes found at the bifurcation of the trachea. The spleen is slightly enlarged; cut surfaces reddish and moderately fibrous. The marrow of the long bones is markedly hyperplastic.

Microscopically the gall-bladder shows a greatly thickened and fibrous wall. The mucosa is desquamated and denuded except in the deeper portions of the crypts. Ulceration extending to the muscularis occurs, and in these areas polymorphonuclear leukocytes and small round cells loaded with bile pigment are numerous. Foreign body giant cells containing bile pigment are also present. Bacteria are numerous; morphologically they resemble staphylococci.

Liver. There is considerable atrophy of the hepatic cells especially about the central veins, so that the capillary spaces are widened. Intracellular pigment is abundant. In certain areas the bile capillaries are hyperplastic and newly formed capillaries are numerous. In other areas there are small focal necroses and distinct patches of scar tissue, which in some instances entirely surround islands of liver cells. In sections stained for bacteria the large amount of pigment obscures the field and no organisms are found.

Bone-marrow. Stained smears disclose well-marked poikilocytosis, anisocytosis, moderate numbers of nucleated red cells, 1 megaloblast, and polychromatophilia.

Bacteriological Findings. Culture not made on account of embalming.

Anatomical Diagnosis. Subacute and chronic ulcerative and endurative cholecystitis with cholelithiasis; numerous fibrous adhesions between gall-bladder and other organs; hyperplasia of bone-marrow; pernicious anemia; focal biliary cirrhosis of the liver with atrophy; fatty and pigment changes; fatty change in the myocardium—"Tiger heart;" petechial hemorrhages in pericardium; moderate emaciation; generalized brownish pigmentation of the skin; moderate atrophy of suprarenal cortex; slight fatty and myxomatous changes in the aorta; calcified tuberculous lymphadenitis; rudimentary right kidney, weight 40 gm.

Case VIII.—(Multnomah Hospital Service). C., aged forty-seven years, was received April 8, 1923. The patient has suffered from a progressing weakness and paleness for more than eight months. Six months ago his hands became numb and soon afterward failing strength in his legs prevented his walking. On entrance he was unable to stand. For two months he has been awakened at night with indefinite pains in the region of the stomach. He thinks he was jaundiced when the pains began but he considers himself jaundiced now. He has had repeated nose bleeding and possibly two chancroid infections. He has lost much in weight.

Examination. The patient is profoundly weak and undernourished though not emaciated. The skin is pale and lemon tinted. The teeth are foul with sepsis and neglect. The tonsils are septic. The tongue is inflamed. There is some generalized lymphadenopathy. There is a discharge from the left ear. A hemic murmur is

heard over the precordium. The patient is considered too weak to make stomach analyses or to study the gall-bladder. There is some increased muscle resistance in the right upper abdominal quadrant; the reflexes are present but weak. The blood Wassermann is negative. Several blood counts show on an average: Hemoglobin, 40 per cent; erythrocytes, 1,640,000; leukocytes, 4800; polymorphonuclears, 62 per cent; small mononuclears, 22 per cent; large mononuclears, 11 per cent; eosinophiles, 1 per cent, transitionals, 1 per cent; questionable myelocytes, 3 per cent; irregular red cells and irregular staining at present. No nucleated red blood cells are found.

Death May 12, 1923.

Autopsy. This is the body of a somewhat poorly nourished white man, aged fifty-one years. The skin, particularly of the face, had a lemon-yellow tinge. The subcutaneous fat is firm and lemon-yellow. There are petechial hemorrhages in root of the mesentery and in the mucosa of sigmoid. The blood is darker red than normal. The gall-bladder is empty and collapsed; it is free from adhesions but its wall is whitish and slightly thickened. The bloodvessels are unusually prominent. It contains a very small amount of stringy brownish bile. The mucosa is intact and there are no concretions. The biliary lymph nodes are small. The larger bile ducts are unchanged. The central veins in the liver are prominent. The spleen weighs 250 gm. The cut curfaces are reddish and firm; Malpighian bodies are visible.

The rugæ of the stomach are lacking; the mucosa is atrophic. The marrow of a portion of the middle third of the tibia discloses a patchy hyperplasia of the blood-forming tissue. The marrow of the ribs is soft and hyperplastic. There are no gross lesions in the brain or spinal cord.

Microscopally the sections of the yellow marrow disclose a moderate hyperplasia of erythrogenetic islands which partially replace the fat. In these islands there are seen megaloblasts, normoblasts, poikilocytes and microcytes and also an increased number of myeloblasts and myelocytes. Phagocytes containing pigment are present. Sections of the red marrow disclose a marked hyperplasia of the blood-forming tissue.

Gall-bladder. The mucosa is intact and normal in appearance. There is a slight diffuse increase in fibrous tissue throughout the wall with scattered round cells in moderate numbers between the fibers. Sections stained for bacteria disclose bacteria for the most part in the form of diplococci.

Spleen. The Malpighian bodies are prominent. The sinuses are engorged with red blood cells in all stages of disintegration. Phagocytes containing broken red cells and pigment are numerous. All types of abnormal red cells are found.

Liver. About the central veins there is almost complete atrophy of the hepatic cells with some faty degeneration. Phagocytes containing brownish pigment and shadows of red cells are seen in these regions. The bile capillaries are unchanged.

Stomach. The mucosa shows well marked atrophy with replacement of fibrous tissue and an infiltration of small round cells and plasma cells.

Heart blood . . .	Pneumococcus in pure culture.
Lung	Pneumococcus in pure culture.
Gallbladder . . .	Pneumococcus and alpha-hemolytic streptococcus.
Bile	Pneumococcus and alpha-hemolytic streptococcus.
Liver	Pneumococcus and Bacilli coli.
Bone-marrow . .	Pneumococcus in pure culture.

Anatomical Diagnosis. Well marked hyperplasia of the red bone-marrow, slight hyperplasia of the yellow bone-marrow; yellowish pigmentation of the skin; petechial hemorrhages in root of mesentery and mucosa of sigmoid; atrophy of gastric mucosa; pernicious anemia; slight chronic diffuse cholecystitis, isolated streptococcus and pneumococcus; syphilitic arteriosclerosis of the aorta; old fibrocaseous tuberculosis of upper right lobe; atrophy and pigment changes in the liver; slight atrophy and fatty changes in the myocardium; moderate hypertrophy of the spleen; lobar pneumonia, lower right lobe; pneumococcus septicemia; sero-fibrino-purulent, right; purulent bronchitis; slight parenchymatous degeneration of the kidneys; interstitial orchitis and atrophy of interstitial cells.

After reviewing the data presented, Dr. Everett O. Jones (Seattle, Wash.) operated on a patient suffering from a frank pernicious anemia, who was under the care of Dr. Edward P. Fick. We are indebted to him for the records of the case, a résumé of which follows:

Case IX.—(The Swedish Hospital, Seattle, Wash., Service of Drs. Jones and Fick). W. J. B., aged fifty-two years, ship captain, had been sick at irregular intervals for three years with weakness, paleness anorexia, diarrhea and numbness above the left knee. One year ago the attack lasted two months. October, 1922, he was delirious for a week during an attack, after which he slowly recovered until January, 1923, when the present relapse began. The patient has used alcoholics to excess. He has spent seventeen years in the Orient and had cholera in 1893.

Examination. The patient is well nourished; the skin pale and lemon tinted; the mucous membranes pale; dental sepsis is severe. The tongue shows no atrophy or inflammation. There is a murmur over the precordium. The stomach shows complete achylia. The reflexes are normal except the knee kicks, which are sluggish. Eight blood examinations were made; one of them is herewith recorded: Hemoglobin, 15 per cent; erythrocytes, 1,200,000; leukocytes,

6000; small mononuclears, 60 per cent; large mononuclears, 40 per cent; 1 normoblast was found in the eight examinations, and the red blood cells show marked anisocytosis and polychromatophilia. The blood Wassermann was negative.

Treatment. It seemed evident that the patient would not survive this relapse, so an exploratory operation was advised and accepted. The gall-bladder was normal in appearance. It was removed and from the gall-bladder wall a pure culture of a hemolyzing Staphylococcus albus was obtained. The bile was sterile.

Death occurred on the day following operation.

Abstract of Autopsy Record. The autopsy was made the same day by Dr. D. H. Nickson. The general appearance of one dead of pernicious anemia is present. Multiple pin-point submucous hemorrhages in the fundus of the stomach exist. The mucosa of the pylorus and first part of the duodenum is markedly thickened and edematous, measuring $\frac{3}{8}$ cm. in thickness. The liver appears normal. The site of the operation is normal; there has been no hemorrhage. The spleen weighs 320 gm. Smears from the spleen pulp show many megalocytes and some nucleated red blood cells. The bone-marrow of the tibia is dark red, hyperemic, and sections show hyperplasia of the elements.

Comment. (N. W. J.) This patient presented during life the course of a frank pernicious anemia. Never had there been any suggestion of gall-bladder disease either before or during his final illness. At operation the gall-bladder appeared to be normal but it was removed and a hemolyzing Staphylococcus albus was obtained in pure culture from its wall. The patient, already approaching his end, was unable to withstand the shock of operation.

Case X.—Mrs. D., aged sixty years, 4 para, was received March 23, 1923. Patient first noticed an oncoming anemia, weakness and loss of weight following the extraction of the teeth for dental sepsis one year ago. These symptoms together with nausea, vomiting, dyspnea, pains in the chest and arms and a recurring soreness of the tongue have been more marked during the last four months. Her past history has been negative.

Examination. The skin is pale and lemon tinted; the mucous membranes are pale; the tongue shows a bright red inflammation about the tip and the dorsum is glossy and fissured. The tonsils are septic. A hemic murmur is heard over the precordium. The stomach shows complete achylia. The stools are negative. The blood Wassermann is negative. Thirteen blood counts were made during the five weeks the patient was in hospital under treatment. The first blood count showed: Hemoglobin, 50 per cent; erythrocytes, 1,990,000; leukocytes, 4200; polymorphonuclears, 57 per cent; small mononuclears, 38 per cent; large mononuclears, 2 per cent;

eosinophiles, 1 per cent; normoblasts, 1; megaloblasts, 2; marked anisocytosis and polychromatophilia. The last blood count showed: Hemoglobin, 75 per cent; erythrocytes, 3,470,000; leukocytes, 3400; polymorphonuclears, 70 per cent; small mononuclears, 28 per cent; large mononuclears, 2 per cent; basophiles, 1 per cent; eosinophiles, 1 per cent; no nucleated red blood cells, and less marked changes in the size and staining of the erythrocytes.

Faint but positive shadows of the gall-bladder were obtained April 30, 1923. There was no distortion or spasm of the duodenum. Operation was performed May 28, 1923. A chronically infected gall-bladder and appendix were removed (by T. M. J.). A small bit of liver was removed for examination.

Pathological Report. The gall-bladder wall is moderately thickened. There is a small amount of viscid bile in the sac. The gall-bladder is partially necrotic (due to delayed examination). Necrosis is too marked for accurate histological study. The wall appears thickened and fibrous. The mucosa is desquamated and the cellular outline is indistinct. Sections stained for bacteria are negative, probably due to autolysis. Sections of the liver show slight necrosis of the cells. Some contain granular brownish pigment. The walls of the capillaries are thickened, due to increase in fibrous tissue in which a few small round cells are present. The epithelium is intact. Sections stained for bacteria show no organisms. Cultures of the bile and gall-bladder are negative. Cultures of the liver show a prolific growth of green producing alpha-hemolytic streptococcus.

Pathological Diagnosis. Chronic cholecystitis and chronic cholangitis.

Course. Convalescence from operation was prompt. The rapid change in symptoms and general appearance noted in the other patients operated upon was observed again. The skin lost its lemon color and became pink. The patient's general sense of feeling became different. (This change has been noted and commented upon by the other patients operated upon.) A very sore glossitic tongue became symptomless within three days. The soreness of the tongue returned, however, after three weeks and still bothers somewhat. The blood before operation showed: Hemoglobin, 75 per cent; erythrocytes, 3,440,000; leukocytes, 5700; moderate changes in size and staining properties of the red cells. On leaving the hospital it showed: Hemoglobin, 85 per cent; erythrocytes, 3,390,000; leukocytes, 5600, and less marked changes in the red cells. And the last examination, August 4, 1923, was: Hemoglobin, 78 per cent; erythrocytes, 2,580,000; leukocytes, 4650, and more marked changes in the red cells.

Comment. This patient represents the type of pernicious anemia characterized by a rapid downward course, with few or no remissions and with many megaloblastic cells in the blood stream.

The same clinical betterment has been noted as in the other patients operated upon and this improvement seems out of proportion to the changes which have taken place thus far in the blood cells. Nevertheless, it is so noticeable to the patient herself that she believes she is going to become well. She bases this upon her increased strength, the fact that she is able to walk up short hills and stairs without shortness of breath and undue fatigue, and that her general sense of well-being has been markedly changed. Although only two months have elapsed since operation and one is not justified to form any conclusions regarding the outcome, still we recognize in this instance, as in the others, a more profound change than we have ever noted in any other form of treatment employed, including splenectomy. Whether the cause of the anemia has been removed or not, nevertheless, the effect thus far seen justifies the hope that some definite modification of the disease has taken place. The streptococcus obtained from the liver tissue undoubtedly existed in the wall of the gall-bladder also.

The brief records of the following 3 patients are also included for the reason that all of them have shown roentgenological evidence of gall-bladder disease. No thought of the existence of such disease would have been seriously considered in 3 of them. In 1 patient recurring attacks of pain and a possible attack of jaundice might have caused the association of gall stones and the anemia to be considered.

Case XI.—Mrs. L., aged fifty-one years, 6 para, was received for the first time October 17, 1914. She had suffered all her life from gastro-intestinal disturbances, vomiting, periods of bowel looseness, fever lasting at times for months, and in later years relapsing periods of paleness and weakness. She had had jaundice in childhood, and tonsil, sinus and dental sepsis for many years. At one time pain in the lower right abdomen led to the diagnosis of chronic appendicitis but she was not operated upon. Later she suffered pain attacks in the left chest. The heart was normal in all examinations except for hemic murmurs heard during relapses. For some years she suffered from numbness, burning and tingling of the hands and feet and of the tongue. Between October, 1914, and June, 1922, the patient was in our care eight times for longer or shorter periods of observation. She suffered from a complete achylia and a severe secondary bowel disturbance. Twenty-three complete counts were made. The persistent characters of pernicious anemia were always present. Nucleated red blood cells were never found. Positive shadows of a diseased gall-bladder with the presence of stones were obtained June 5, 1922. Cholecystectomy was urged at that time as a possible relief for the anemia but was not accepted.

Death occurred during a relapse at her home in an adjoining state, in March, 1923.

CASE XII.—Mrs. McP., aged forty years, 1 para, was seen June 20, 1922. Patient had complained for a year of exhaustion. Constipation had existed for fifteen years and the skin had been sallow for a long time. Once for a short time, one year ago, and lately for six weeks, patient has had some dull distress in right upper abdomen. She has had a dental sepsis. The tongue is negative; the stomach shows complete achylia. There are no paresthesiæ. Two blood examinations show: Hemoglobin, 90 per cent; red blood cells, 3,400,000; white blood cells, 5000. The red blood cells show a moderate number of megaloblasts and some polychromatophilic staining. There are no nucleated red blood cells. The blood-Wassermann is negative. Positive gall-bladder shadows, without evidence of stones, are obtained on the films. Operation is not accepted.

CASE XIII.—Mrs. E., aged sixty-three years, 6 para, was received March 22, 1923. Since an acute illness two years ago the patient has been developing an increasing weakness and paleness; constipation exists but no bowel looseness. Soreness and burning of the tongue have been present for the last two weeks. Parasthesiæ have been absent. There is an old history of dental sepsis. The patient has a marked lemon-tinted paleness of the skin, glossitis, complete achylia and a megaloblastic blood picture. Positive gall-bladder shadows with stones are obtained. On entrance to hospital the blood examination showed: Hemoglobin, 42 per cent; erythrocytes, 1,680,000; leukocytes, 3200 and numerous normoblasts and megaloblasts. She remained one month under treatment in preparation for a cholecystectomy but finally refused operation. On leaving her blood showed: Hemoglobin, 70 per cent; erythrocytes, 2,500,000; leukocytes, 3400; 1 normoblast, fewer macrocytes and no megaloblasts.

Discussion. In the accounts of the 13 cases there is presented certain clinical, operative and postmortem evidence pointing to the fact that idiopathic pernicious anemia is related to and possibly caused by the action of hemolytic or other microörganisms which have invaded the wall of the gall-bladder and from this organ as a focal site are producing their effect upon the red blood cells and erythrogenetic centers of the bone-marrow. In the 10 operated or autopsied cases the wall of the gall-bladder afforded organisms by culture or by staining the tissues, or by both methods. In the 7 instances in which cultures were obtained hemolyzing organisms were found in 4, alpha-hemolytic streptococcus in 2 and non-hemolytic Staphylococcus albus in 1. In Cases III and IX hemo-

lytic Staphylococcus albus was obtained and in each instance it was believed to be a pathogenic organism and not one of contamination. Case IX is of special note for the pathological and bacteriological examination was made by other observers and in-so-far as one case may decide it serves as confirmation of our own observations. Case VIII is also of special interest because in the presence of a terminal pneumococcic septicemia; an alpha-hemolytic streptococcus was obtained locally from the gall-bladder wall. The organisms lie most abundantly in the areas of scar tissue within the muscularis where possibly a lowered oxygen tension permits of a better growth. In this respect it reminds one of the localization of Streptococcus viridans in the leaflets of the heart valves in subacute infectious endocarditis. It raises the query whether or not the organisms may be able to seal themselves up within a suitable medium that permits growth over a long period of time and thus allows an organism of low virulence to produce death of the host after many months or years, even as the Streptococcus viridans does in the heart. In Cases IV and X a bit of liver tissue gave a pure culture of alpha-hemolytic streptococcus. In none of the autopsied cases have organisms been thus obtained. They also have not been found in sections of the liver stained for bacteria, but the presence of pigment obscures the picture. Whether these organisms will be universally found in the liver substance, as Graham[17] has shown in ordinary cholecystitis, remains to be determined.

The macroscopical appearance of the gall-bladder is important. In Cases III and IX it was considered normal by the surgeon. In Cases II, IV, V, VIII and X the macroscopical evidence of disease was slight. In Case VI an unsuspected gall stone was found at autopsy. In all cases studied roentgenologically by Dr. Palmer for the presence of chronic gall-bladder disease sufficient proof was found to justify the removal of the organ. This emphasizes again the contention that positive gall-bladder shadows are more conclusive of disease than the macroscopical appearance of the gall-bladder at operation. In only 1 case of the series (Case I) was there sufficient clinical evidence to justify the thought that chronic gall-bladder disease might be present.

From the therapeutic standpoint there is much to be learned that only the experience which comes with time will teach. If these observations are proven to be true in a reasonable percentage of cases, it would seem justifiable to perform cholecystectomy in those instances, at least, in which roentgen-ray evidence of gall-bladder disease is obtained. Indeed, if suitable roentgen-ray studies are not available, it might still be proper to remove the gall-bladder inasmuch as we are dealing with an incurable disease. With a record of only 5 operated patients but little may be said. One patient has lived for six years after operation with apparent abeyance of those

symptoms of pernicious anemia from which she suffered at the time of operation. The second patient was suffering from a severe and frank although slowly progressing pernicious anemia. The result of operation in his case after eleven months' time is certainly all that could be hoped for. One must not wait for the appearance of megaloblastic cells in the blood stream or the presence of cord changes before thinking of pernicious anemia. If the disease is caused by various organisms of special characters and of different degrees of virulence the variations in its clinical course are easily understood, and the earlier treatment is instituted the more perfect may be the end-result obtained. A case in point is the following: A strongly built woman, aged fifty-seven years, began in November, 1922, to have nausea and vomiting. Two months ago an annoying flowing of saliva and a distressing soreness of the mouth began, which were laid to the door of septic teeth and tonsils. These were removed. About the same time one hand became numb. A recent examination of the patient did not reveal any local cause of the salivary disturbance within the head. The chemistry of the stomach was normal. The blood examination showed hemoglobin 100 per cent and red blood cells 4,900,000. There were some macrocytes present. Positive proof of a gall-bladder disease was obtained. With this combination of subjective symptoms and gall-bladder disease a beginning pernicious anemia may well be considered *

One more point in regard to the treatment of these cases may be mentioned. For over twenty years large doses of arsenic, especially of sodium cacodylate, have been empirically used with benefit in the treatment of streptococcic infections. For a much longer time arsenic has been the most efficient means employed in prolonging the life and alleviating the suffering of the patient with pernicious anemia. The underlying reason may be the same because of the inhibiting power which arsenic has on these organisms. We have safeguarded our operative results by treating the patient in bed with arsenic to the point of physiological tolerance, forced feeding and hydrochloric acid. With each patient we have aimed to raise the hemoglobin content above 70 per cent, the red cell count to 3,000,000 and to add several pounds to the weight before operating, and then to operate before the beginning of another relapse. The 1

* Cholecystectomy and appendectomy was performed on this patient June 14 (by E. W. St. P.). The pathological report is as follows: The gall-bladder wall is slightly thinned, the mucosa atrophic sections show thinning of the wall, slight fibrosis of the muscularis, atrophy and desquamation of the epithelium of the mucosa. In the wall are some large lymphocytes and small round cells. Sections stained for bacteria show the presence of a few diplococci and intracellular cocci. The bit of liver tissue is not sectioned. Cultures of the bile, the gallbladder and the liver are negative.

Pathological Diagnosis. Chronic atrophic cholecystitis. *Course.* Convalescence from the operation was normal. The drooling and the numbness of the hand practically disappeared before the patient left the hospital.

death recorded occurred in the wake of a relapse. It is not unlikely that an exaggerated risk may be present at this time, although the experience of splenectomizing such patients does not wholly bear out this view.

Experimental work has been started in the pathological laboratory in an effort to determine whether some of the organisms isolated from the gall-bladders of pernicious anemia patients are pathogenic for animals. It is the purpose also to determine if possible whether pernicious anemia is caused directly by the lytic action of bacteria and their products on erythrocytes, or whether the anemia may be the effect of some chemical substance entering the circulation from the infected gall-bladder. The fact that the lytic substances causing the pernicious anemias of Bothriocephalus latus and of hookworm infections are lipoid in character, and that a megaloblastic anemia may be produced experimentally in rabbits by using a similar agent, suggests the possible changes in the cholesterol content of the bile, especially within the gall-bladder, by means of organisms possessing special properties as being the cause of another group. These studies will be reported later.

Conclusions. 1. Evidence is brought forth pointing to the presence of hemolyzing and other microörganisms in the wall of the gall-bladder as being the possible cause of idiopathic progressive pernicious anemia.

2. In a series of 13 cases the presence of chronic gall-bladder disease was found by special study in each one.

3. Cholecystectomy on 5 patients of this series seemingly has removed some or all of the symptoms of the disease.

BIBLIOGRAPHY.

1. Addison: Idiopathic Anemia: On the Constitutional and Local Effects of Diseases of the Suprarenal Capsules, London, 1855.
2. Biermer: Cor.-bl. f. schweiz. Aertze, 1872.
3. Hunter: Brit. Med. Jour., March 18, 1922, 421.
4. Schaumann and Tallqvist: Deutsch. med. Wchnschr., 1898, **24**, 312.
5. Schaumann: Akademische Abhandlung, Helsingfors, Weilin and Goos, 1894, p. 214.
6. Faust and Tallqvist: Arch. f. exp. Path. u. Pharmakol., 1907, **57**, 367.
7. Ashford and King: Jour. Am. Med. Assn., 1907, **49**, 471.
8. Whipple: Jour. Exp. Med., 1909, **11**, 333.
9. Bunting: Johns Hopkins Hosp. Bull., 1900, **16**, 222; Jour. Exp. Med., 1907, **8**, 625; Jour. Am. Med. Assn., 1907, **49**, 476.
10. Madler: Jour. Med. Res., 1913, **28**, 199.
11. Eppinger: Berl. klin. Wchnschr., 1913, p. 1553; 1913, p. 2409.
12. v. DeCastello: Wien. klin. Wchnschr., 1913, **26**, 951.
13. Georgi: Berl. klin. Wchnschr., 1887, p. 822.
14. Ewald: Berl. klin. Wchnschr., 1887, p. 850.
15. Percy: Surg., Gynec. and Obst., 1917, **24**, 533.
16. Giffin and Bowler: Minnesota Med., 1923, **6**, 14.
17. Graham: Surg., Gynec. and Obst., 1918, **26**. Graham and Peterman: Arch. Surg., 1922, **4**, 23. Peterman, Priest and Graham: Arch. Surg., 1921, **2**, 92.

DIABETES SURGERY.

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Few diseases require a closer coöperation between surgeon and internist than does diabetes. The type of coöperation called for demands on the part of the surgeon, at least a fairly comprehensive knowledge of the work that has been done and is being done, in metabolism studies of blood and urine; and on the part of the internist, an appreciation of the refined judgments of the surgeon, attempting to determine whether or not a patient with a simple uncomplicated diabetes should be subjected to operation for a lesion unrelated to his glycosuria; or whether a diabetic patient with a surgical complication is able to withstand the life-threatening dangers incident to operative interference.

In the instance of diabetes, as in the case of quite a large number of diseases that may require surgical treatment, the facts of most fundamental importance have been developed by internist, physiologist, pathologist, and chemist. It would seem almost to be an affront for a surgeon to emerge from within his charmed circle of pure technic. The fact of the matter, however, is that the real surgeon strives most zealously to comprehend, to appropriate and to apply properly the principles discovered by his colleagues in other branches. In this process of comprehension, appropriation and application, it not uncommonly happens that the humble surgeon contributes his mite, both to science and to suffering humanity.

Twenty years ago, the problem of surgery on diabetics was a fairly simple one. It was then generally conceded that the dreaded postoperative coma could be best averted by a fairly liberal carbohydrate intake just before, and as soon after operation as possible. Diabetes was, of course regarded as a possible *nolle me tangere*, and consequently, operative indications were set prayerfully, and with due consideration; but the chemistry involved in acidosis, the question of the combining power of the blood for CO_2, the problems of the chemistry of blood sugar, and of the influence of the fat solvent power of ether as a prime factor in the production of coma, all these problems were just beginning to be linked to clinical medicine. Twenty years ago, the American surgeon operated upon a diabetic patient reluctantly, placed much faith in the use of carbohydrate feeding, and then awaited the outcome with the spirit of a hopeful fatalist who had at his command at least one powerful aid—asepsis.

In 1913, Kaposi published a very exhaustive clinical and bibliographical study of surgery in diabetes. He was able to collect

less than one hundred titles covering a period of the preceding twenty-five years. This is a fairly safe index of the dearth of knowledge of the subject, up to ten years ago; for there is a great tendency to appear in print, on the part of those of us who only presume that we have something worthwhile to say. Even in this scanty literature, there were many conflicts. For example, one surgeon, Sternberg, said that any necessary operation may be performed with safety, on a diabetic. Other surgeons (Lepine and also Kausch) said that every operation is contraindicated in diabetes. Da Costa said that the increased sugar content of the blood made it a favorable culture medium, and that operation wounds in diabetics were therefore frequently infected. Handman, on the other hand, explicitly refuted this statement, and showed that the growth of staphylococci was the same in diabetic as in non-diabetic blood, that the bactericidal power of blood is not influenced by the addition of 1 per cent of sugar, and that its opsonic index likewise, is not influenced. Surgeons in general, had a wholesome fear of postoperative coma in any diabetic patient; and yet, Manges concluded that, "The surgeon has too much fear of acidosis. There is no danger, no matter how intense the acetone reaction may be, when the diacetic acid or the oxybutyric acid tests are negative."

From conflicting opinions such as these, it is not warrantable to draw the conclusion that fifteen or twenty years ago, the problem of surgery in diabetes was in a state of chaos. Certain principles governed the thoughtful surgeon—principles that maintain even today, except for those modifications that have resulted from the introduction of insulin. In the first place, it was recognized that diabetes was a disease varying in severity from the mild to the severe, and that the results of surgical interference were measurably proportionate to the grade of the disease. It was regarded as true von Noorden's axiom that: Every diabetic is, emphatically, less resistant to trauma (including surgical trauma) than is a non-diabetic patient. It was known that anesthesia was a precipitant factor in the production of coma, that wound healing was proudly affected by a high blood-sugar content, that wound infection was to be feared, and that immunity to infection in general was low in diabetes. Finally, and most important of all, it was known that not only were special tissues compromised, but also, that the organism as a whole was weakened by diabetes. The frequency of endarteritis, myocarditis and neurotrophical disturbances, the not uncommon loss of weight, and the frequent existence of nephritis were facts of common knowledge to the surgeon. They counted much more with him than did academic discussions as to the whys and wherefores of their existence.

During the past ten years a voluminous amount of work has been done on the very fundamental problems of blood-sugar and blood-fat content, on ketonuria, on the CO_2 combining power of the blood,

on the reactions of renal epithelium to blood sugar, on the broad general problem of carbohydrate metabolism in its relation to diabetes. Although this work has not appreciably altered the practical relationships between surgery and diabetes, it is nevertheless necessary for the surgeon to be in possession of the new fundamental facts, if he hopes to set surgical indications correctly.

He must know that in the fasting normal individual, the blood contains 0.1 per cent of sugar. It is much more important for him to know that this is not a fixed percentage. A perfectly normal individual may have as much as 0.16 per cent, or even a somewhat higher percentage. Hamman and Hirschman believe that the renal threshold for sugar is 0.17 per cent to 0.18 per cent of blood sugar. When the percentage of blood sugar rises above the normal limit, the sugar passes through the kidney and appears in the urine. That point of concentration of blood sugar at which the first trace escapes through the renal epithelium, and appears in the urine, is known as the "kidney threshold." The process of escape has been referred to as "renal leak." Both these phrases, though connotative of a purely mechanical process, are, in reality, not intended to convey the idea that the kidney is a mechanical filter. The process is, in some respects, analogous to that of filtration but an exact explanation of just how it occurs has never been furnished.

When a patient has a definitely normal percentage of blood sugar and nevertheless shows sugar in his urine, we are inclined to class him among the cases of so-called renal diabetes, and to consider him as a subject whose renal epithelium is, for some reason or another abnormally permeable to sugar. It is questionable whether this group of patients are unqualifiedly better operative risks than are those individuals suffering from essential diabetes.

There is another group, in which almost the opposite condition exists, that is, an abnormally high blood sugar, with no sugar in the urine. From the point of view of surgical disaster, this last mentioned group is menacing. Not infrequently these patients give a history of having been rather casually and yet, seemingly successfully treated for diabetes. Frequently, the story is that, some time in the past, they took one or more cures at Carlsbad, and have shown little or no sugar, since the last treatment, a year or more in the past. Urinary examination confirms the absence of sugar, the patient seems to be a good operative risk, but nevertheless, operation is followed by coma. Two years ago, just such a patient of mine, after a simple colostomy for cancer, was rescued from profound coma by persistent and rather heroic intravenous administration of dextrose. The colostomy was done under local anesthesia. This particular patient, in common with most of the patients in this group, had nephritis of mild grade. It is commonly assumed that a nephritis tends to raise the renal threshold of sugar, so that as the nephritis manifests itself more and more, the glyco-

suria becomes less and less pronounced. Mosenthal contests this view however, and says that the threshold for sugar is raised by many factors other than nephritis, and that in some instances, nephritis is accompanied by a distinct lowering of the kidney threshold.

Whether nephritis, raises, lowers or does not influence the kidney threshold, is not in itself, of vital importance to the surgeon. On the other hand, it is vitally important for the surgeon to recognize the three facts that:

1. The blood sugar may be within normal limits, and be accompanied or unaccompanied by glycosuria.
2. The blood sugar may be abnormally high, and be accompanied or unaccompanied by glycosuria.
3. The blood sugar may be abnormally low, and be accompanied or unaccompanied by glycosuria.

I say that a knowledge of these facts is of importance to the surgeon, because they prompt him to ask, "If high blood sugar does or does not produce sugar in the urine, and if likewise, low and normal percentages of blood sugar does or does not produce sugar in the urine. Just what shall we consider diabetes to be?"

We have the right to ask this question, but I doubt if there is warrant to hope for a categorical answer. My very worthy, competent and in some instances, authoritative internist friends, very properly refuse to commit themselves, when I ask for a definite opinion as to the operative risk in the instance of a surgical patient with 0.2 per cent of blood sugar, and no sugar in the urine. For myself, I believe that we surgeons should consider such patients as not merely possible, or as potential, but as real diabetics; and that we should set both our operative indications and our postoperative treatment accordingly. It is necessary for us to remember that glycosuria, as a symptom, is of importance in that it is an indicator of hyperglycemia. Hyperglycemia is the root of all evil in diabetes, and however unwilling we may be to dogmatize in figures, we cannot go wrong, if we decide to regard as diabetics, all individuals whose blood sugar is 0.2 per cent, on ordinary diet, and 0.16 fasting, even though the urine contain no sugar.

Considering the above fundamental fact as established, we may next consider the purely surgical aspects of diabetes. Such a consideration will be simplified by grouping the surgical patients under the following three heads:

1. Those whose diabetes is merely an incident of seemingly lesser importance, and who seek advice regarding the performance of an operation for the relief of an unrelated condition, such as hernia, uterine fibroids, cholelithiasis, hypertrophied prostate, or less grave lesions.
2. Those who suffer from gangrene, either of the extremities or elsewhere.

3. Those who suffer from surgical infection, such as surface infections (carbuncle, furuncle, cellulitis) or from visceral suppuration of a grave nature (appendicitis, lung abscess, strangulated hernia, or any type of intra-abdominal suppuration).

Although insulin has been used for only a comparatively short time, the conclusions seem warrantable that this drug fairly guarantees against the development of coma, aids much in raising the natural resistance against infection, and probably, insures better wound healing. According to Foster, a fatal result inevitably follows major operations performed on patients whose blood sugar is over 0.35 per cent, or whose blood CO_2 combining power is less than 40 per cent. Insulin corrects both of these complications, and in so doing, has conferred probably its greatest boon on surgery. For years, surgeons have experienced the mingled sensations of hopeful expectancy and timid apprehension, hopefully expectant that some such substance as insulin would be discovered, and apprehensive that it might not be in his day.

Conceding, without qualification, the indispensability of insulin to the surgeon, the important fact remains, that before a judgment may be reached regarding the surgical treatment of a diabetic, it must be borne in mind that diabetes is a constitutional disease, affecting not only special tissues, but also the body as a whole; that this compromise of the body manifests itself by a lowered resistance against infection and trauma, by a consequently unpredictable course of wound healing, by an extraordinary incidence of undesirable postanesthetic sequellæ, such as acidosis, coma, pneumonia, and finally, by an increased incidence of undesirable postoperative sequelæ, such as thrombosis, embolism, cardiac failure and grave asthenia.

Even insulin does not furnish an escape from these facts, facts emphasizing the special surgical hazards to which diabetics are exposed. Those patients whom we have placed in Group 1, the ones with hernia, fibroids, or other lesions unrelated to diabetes, should be subjected to operation, only when good judgment measures the disability or danger incident to the surgical disease, as greater than the risk of operating upon a diabetic. This statement affords, of course, a wide latitude of opinion; but it nevertheless stresses the fact that these patients, in Group 1, are poorer surgical risks because they are diabetics.

The patients in Group 2, those with gangrene, constitute a very distinct set. The gangrene most commonly affects the lower extremities, and is always referable to a lessened blood supply, secondary to arteriosclerosis, with endarteritis, and not infrequently, with embolus or thrombus formation. The exact role that the diabetes plays, in the production of the vascular changes is still more or less problematical, though there seems to be a direct causal relationship between diabetes and arteriosclerosis. The most strik-

ing, and one of the most important facts in connection with these peripheral gangrenes, is the marked disproportion that exists, so frequently, between the slight extent of the gangrene, and the marked degree of involvement of the vessels of the leg. I have repeatedly seen a gangrenous area only a half a square centimeter in area, at the end of a toe, accompanied by an almost incredible degree of thickening and calcification of the arteries of the thigh and leg, from Hunter's canal downward. This state of affairs occurs in the non-diabetic, as well as in the diabetic gangrenes. Equally striking is the frequency with which these seemingly insignificant gangrenous lesions occur in legs, in which the popliteal artery is completely thrombosed at its bifurcation. In an extremity of this sort, amputation below the site of vascular obstruction is generally not only useless, but is frequently hazardous, on account of the subsequent gangrene of the stump.

Peripheral gangrene of the extremity usually calls for amputation and the amputation must usually be done in the supra-condylar region, or higher. It is possible that a fortuitous circulation may permit more conservative treatment. In some instances, a definite line of demarcation forms at the base of a toe, and is followed by the spontaneous sloughing of the toe, and subsequent healing. I have seen this outcome in diabetic gangrene only once and I have seen it very seldom in arteriosclerotic gangrene of the non-diabetic variety. Good fortune has rarely smiled on my efforts to proceed conservatively with diabetic gangrene of the extremities. One should not oppose conservative methods, in any case where they offer hope; but one should be careful lest false hope handicap the patient with the dangers incident to delay. In those cases, where the gangrene is overshadowed by a complicating cellulitis and lymphangitis, it is almost always wise to devote a rational amount of time to an attempt to cure the infection, or at least to check its spread, before amputating. Such time is not wasted, for the interval may be used in regulating the carbohydrate metabolism with insulin, diet and other corrective methods.

The gangrenes other than those that occur in the extremities, are practically always due to trauma, to infection, or to both of these factors. Such a spreading gangrene of skin and soft parts, may originate in an innocent pimple, or after a hypodermatic injection or an insect sting, or after a more serious contusing trauma. For this type of gangrene, there is little to do, except to practise conservative methods. If a line of demarcation forms, excision is usually not necessary; and if a line of demarcation does not form, the surgeon cannot know where to anticipate it. In such cases, as in every instance of surgery on a diabetic, the fundamental indication for insulin and dietary regulation must be met.

Finally we come to Group 3, those patients suffering with carbuncle, furuncle, cellulitis, or visceral suppuration. Practically all

of these patients require more or less operative surgery, preceded, in some instances by such conservative measures as rest, suitable posture, and warm moist packs. From the practical surgical point of view, it makes little difference whether the infection is the result of hyperglycemia, or of lowered tissue resistance; because insulin plus dietary measures corrects both these abnormalities, and markedly increases the patient's chances to withstand infection and surgical trauma.

Nothing said at this time, regarding the preoperative preparation, and the postoperative care of diabetic patients may be regarded as final, because we are still in process of feeling our way with insulin. The procedure that I am now using, varies somewhat with the degree of urgency of the operative indication, and is largely patterned after the ideas of Joslin.

If operation may be deferred a few days, and the patient shows marked glycosuria, ketonuria, and hyperglycemia, he is immediately put on a diet moderately reduced in carbohydrates and proteins, and markedly reduced in fats. Insulin is immediately started, with one unit before the first meal, two units before the second meal, and so on, until five units are given three times daily, before meals. The urine is examined two hours after each meal. The diet is reduced daily, the fats being cut out entirely, very early in the reduction. At that point where the sugar disappears from the urine, further dietary reduction ceases, and the patient continues to receive five units of insulin, three times a day. Gradually the diet is increased, until the full caloric needs of the body are met, provided the urine remains sugar and ketone free. If sugar appears before the body's caloric needs can be met, and if it cannot be eliminated by reducing the carbohydrate, and increasing the protein and fat intake, then one unit of insulin is given for every one and a half grams or total sugar output in the urine. If the ketone bodies alone appear in the urine, then the protein and fat intake is lowered, and the carbohydrate and insulin administration allowed to remain stationary; or, the protein and fat intake remain stationary and the carbohydrate and insulin administration is increased. On the morning of the operation, the patient is given 60 gm. of glucose and at the same time enough insulin to oxidize this amount of glucose, that is, one unit of insulin for every one and a half units of glucose.

If operative interference is imperatively urgent, the patient is given 60 gm. of glucose and at the same time an oxidizing dose of insulin, and then the operation is performed. Coma is avoided by the active oxidation of carbohydrates (not necessarily the patient's own carbohydrates) and the rationale of the joint administrations of glucose and insulin lies in the fact that active oxidation is assured and at the same time enough carbohydrate is administered to protect against a possibly dangerous hypoglycemia.

Summary. The results of proper treatment are usually threefold: (1) A drop in blood sugar; (2) a drop in ketone bodies, or a disappearance of them; (3) an increase in the alkali reserve, with consequent increased combining power of the blood for CO_2. These highly desirable results may be counted upon with more certainty, if the condition of the patient permits a six-hour delay in operating, so that the glucose and insulin administration may be repeated.[1]

THE CLINICAL UTILIZATION OF LEUKOCYTE COUNTS WITH SPECIAL REFERENCE TO THE USE OF GRAPHIC REPORTS.

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The first enumeration of the cellular elements of the blood, according to Gray,[1] was made in 1851. Since that time methods have been so perfected, and the results so well evaluated that blood counts are almost the most frequently utilized of all clinical laboratory procedures. In spite, however, of the extensive literature which has accumulated concerning the cytological blood examinations and the significance of the normal and abnormal variations thus demonstrated; in spite of the volumes which have been written upon the interpretation and significance of the findings thus obtained, there are times when it seems as if the resulting data do not attain their full clinical utilization.

Laboratory requisitions for blood counts are, as a rule, concerned merely with a tabulation of the numerical findings; particularly is this the case with the total and differential counts of the white cells; the degree to which these figures are correlated with the clinical data and utilized as a diagnostic and prognostic aid being directly proportionate to the acumen, experience, and reading of the clinician to whom they are reported. The purpose of the present communication is to call attention to some of the methods of graphically correlating the data obtained by white blood cell counts with the clinical data and to emphasize the clinical value of such reports.

It is a matter of common knowledge that in the majority of acute infections the severity of the process is indicated to a greater or lesser degree by the percentage of the polymorphonuclear leukocytes, while the total white cell count may be taken as a fairly accurate

[1] I am indebted to Dr. Albert E. Taussig, Chief of the Medical Service, and to Dr. C. M. Wilmhelmj, for their coöperation in working out this problem of preoperative preparation.

[1] Cell-counting Technic: A Study in Priority, Am. Jour. Med. Sci., 1921, **162**, 595.

index of the ability of the patient to combat the infection; and while these statements are in large measure true and the inferences to be drawn from them may be largely relied upon, a blind reliance upon such deductions cannot be countenanced. Alterations in the total and percentage number of the white blood cells as a response to infections are dependent upon: (1) The stimulus arising from the infection, and (2) the ability of the patient to respond to stimuli. Undue importance, therefore, cannot be placed upon one method of enumeration to the exclusion of the other; while both the total and differential counts are individually informative, the sum total of the information obtained from both together is vastly greater than that obtainable from either alone. If, for one reason or another, a choice must be made, the taking of a smear for a differential count is to be preferred as giving the greater information and, in addition, permitting of some study of the morphology and characteristics of the erythrocytes.

Leukocytosis. The majority of observers place the normal total white cell count as between 7000 and 10,000 per c.mm. and any increase beyond these figures is looked upon as a variation from the normal, and constituting a leukocytosis without, however, such variation being necessarily of pathological origin.

There are numerous factors capable of causing variations in the total white cell count, some dependent upon technical details, others of so-called "physiological" origin, and, finally, those having a pathological basis.

Among the technical factors, which must be especially guarded against by those making such examinations infrequently, may be noted: (1) Dilution of the blood by undue squeezing of the part from which the specimen is taken; (2) concentration of the blood by undue and unduly prolonged constriction of the part; (3) failure properly to mix the blood and the diluent before making the count.

Among the factors of physiological origin are:

1. Digestive leukocytosis, by which is meant the increase in the total number of leukocytes following the ingestion of food. This, at times, may be quite marked, but as a rule the counts are in the neighborhood of 10,000 to 12,00 per c.mm. This type of leukocytosis usually comes on within an hour after the ingestion of food and may extend over a period of three to five hours.[2] While the increase is mainly of polymorphonuclear cells, there is also an increase in the absolute number of small mononuclear cells. It has been shown that the degree of digestive leukocytosis is influenced by the amount of protein ingested, vegetables and fat having a much less marked effect. Owing to the marked fluctuation in this type of leukocytosis it has been suggested—and with reason—by Mauriac and

[2] Webster, R. W.: Diagnostic Methods, seventh edition, Philadelphia, P. Blakiston's Son & Co., p. 608.

Cabouat[3] that it should be called digestive leukocytic fluctuation rather than digestive leukocytosis. This normal occurrence is the starting point for the crise hemoclasique of Widal to which reference will be made later. Just as under other circumstances, the leukocytic response to digestive activities may be more marked in children than in adults.

2. For reasons as yet not quite clear, pregnancy may be associated with increases in the total white cell count, sometimes reaching as high as 15,000 per c.mm.

3. A leukocytosis of from 15,000 to 20,000 per c.mm. may be found in the newborn due to a combination of factors, in which rapid blood formation and the influence of feeding are the most prominent. It is to be remembered that children are apt to show a more marked leukocytic response to stimuli than adults and that especially the percentage of small mononuclear cells seems to be more easily influenced in children.

4. Drugs, exercise and cold baths may also be responsible for an increase in the white cell count which, however, is transient in character.

Among the drugs responsible for increased leukocyte counts may be noted, quinin, camphor, turpentine, drugs of counterirritant properties, tuberculin, potassium chlorate, and thyroid extract.

In the consideration of leukocyte counts it is important to bear in mind:

1. A single count represents merely the condition at the time the count was made. The greatest value is obtained from the composite picture of several successive counts made at intervals of not less than two hours.

2. An increasing or sustained leukocytosis is of more diagnostic and prognostic value than the findings of an isolated examination.

3. The degree of leukocytosis is related as much to the ability of the patient to react as to the stimuli applied.

4. The presence of persistent leukocytosis is against the benignity of any tumor and a steadily increasing leukocytosis in malignant disease is significant of rapid growth or metastasis.

Daland,[4] after a study of 100 normal individuals and 100 cases of the condition in question, concludes that a lymphocytosis may be taken as a diagnostic sign of chronic periapical dental infection in adults, especially when this occurs in the presence of a coincident leukopenia.

The association of a leukocytosis with internal hemorrhage has again been emphasized very recently.[5] The factors responsible

[3] Paris méd., 1921, **11**, 407 (quoted by Webster, Note 2).

[4] Lymphocytosis as a Diagnostic Sign of Chronic Periapical Dental Infection in Adults, Jour. Am. Med. Assn., 1921, **77**, 1308.

[5] Leukocytosis following Internal Hemorrhage, Editorial, Jour. Am. Med. Assn., 1923, **81**, 479.

seem to be associated with initial clotting and with the entrance of the blood into a serous cavity as shown by the work of Wright and Livingston,[6] who demonstrated that intraperitoneal and subdural hemorrhage are always associated with a leukocytosis reaching its maximum about ten hours after the occurrence of the hemorrhage and showing a slow drop to normal over a period of several days following. Levinson[7] has also emphasized the necessity of remembering in abdominal conditions that a leukocytosis is not necessarily indicative of sepsis, as it also occurs with abdominal hemorrhage.

Evans[8] has recently noted a possible prognostic value for the differential count in pernicious anemia. He shows that the increase in the antihemolytic power of the blood whereby remissions occur in this disease is frequently associated with an increase in the percentage of polymorphonuclear cells and that this finding may be utilized to foretell the approach of a remission or *vice versa*. He ascribes the polymorphonuclear leukocytosis to a probable improvement in the bone-marrow function.

Simon[9] emphatically endorses what he speaks of as the "septic factor:" An absence or decrease in the number of eosinophiles associated with an increase in the percentage of polymorphonuclear neutrophiles and which he finds to be almost invariably present in pyogenic infections.

He believes that, in a supposed infection of this character, if, in the presence of an increased number of polymorphonuclear neutrophiles there is a normal or increased number of eosinophiles, the inference is warrantable that either the diagnosis is wrong or that the condition is being successfully overcome.

He also gives a useful table indicating the more common conditions in which the white cell count is increased, which is reproduced in Table I.

Jones and Brown[10] hold the opinion that an increase in the percentage of lymphocytes, if not excessive, is a favorable sign, while a decrease below the normal is of unfavorable import.

Graphic Methods of Representing the Significance of Leukocyte Counts. Of these there are several which are often of signal value in following the course of a particular case and which present the evidence more vividly than can be grasped from a succession of laboratory reports, each bearing the statistical results as usually reported. To obtain the greatest value from leukocyte counts,

[6] The Leukocytosis of Internal Hemorrhage, New York State Med. Jour., 1923, **23**, 286.

[7] Leukocytosis, a Deceptive Sign in Abdominal Hemorrhage, Jour. Am. Med. Assn., 1915, **64**, 1294.

[8] Subjective Symptoms and the Differential White Blood Cell Count as aids in the Prognosis of Pernicious Anemia, Pennsylvania Med. Jour., 1923, **26**, 228.

[9] Clinical Diagnosis, tenth edition, Philadelphia, Lea & Febiger, p. 50.

[10] The Clinical Significance of Total and Differential Leukocyte Counts with Special Reference to Acute Infections, Am. Jour. Med. Sci., 1922, **164**, 607.

especially as a means of recording progress, it should be emphasized again that they should be made in series.

TABLE I.—MORE COMMON CONDITIONS IN WHICH CHANGES IN THE LEUKOCYTES ARE FOUND.

A. Neutrophilic Hyperleukocytosis.	B. Neutrophilic Leukopenia.	C. Lymphocytosis.
All pure infections with:	Typhoid fever	Acute and chronic lymphatic leukemia
Streptococci	Paratyphoid fever	Pertussis
Staphylococci	Measles	Rickets
Pneumococci	Chronic, subacute tuberculosis	Congenital syphilis
Meningococci	Influenza	Measles
Catarrhal micrococci	Pernicious anemia	Typhoid fever
Colon bacilli	Splenic anemia	Tuberculosis
(Hence the common wound infections)		Influenza
Pneumonia		Paresis
Erysipelas		Diseases involving ductless glands
Meningitis		
Appendicitis		
Peritonitis		
Tonsillitis		
Salpingitis		
Puerpera sepsis		
Diphtheria		
Acute rheumatism		
Empyema		
Various abscesses		
Cancer, with ulceration		
Hemorrhage		
Poisons		
Toxemia (bacterial or of food origin)		
Anaphylaxis		

D. Lymphopenia.	E. Hypereosinophilia.	F. Hypoeosinophilia.
The various diseases associated with an increase in the polymorphonuclear neutrophiles	Myelocytic leukemia	Noted in all the conditions mentioned in Column A
	Bronchial asthma	
	Scarlatina	
	Various skin diseases	
	Helminthic infestations	
	Gonorrhea	
	Active tuberculosis	
	During convalescence from pyogenic diseases mentioned in Column A	

G. Splenocytosis.	H. Hyperbasophilia.	I. Myelocytosis.
Rickets	Asiatic cholera	Myelocytic leukemia
Syphilis	Myelocytic leukemia	The various pyogenic infections noted in Column A
von Jaksch's anemia		Pernicious anemia
Typhoid fever		Severe secondary anemia
Smallpox		
Mycosis fungoides		
Chronic malaria		
Kala-azar		

A simple chart is readily improvised from the usual squared paper used for temperature or similar records by marking the cross-lines with figures representing the white cell count in thousands, beginning at 6500 and running to 30,000 in multiples of 1000. A graphic record of the rise and fall of the total white cell count is thus readily obtained which shows many things at a glance. This method, of course, is crude and simple, but is better than none. Many more valuable are obtainable but do not seem to have come into use as widely as they should.

Another simple form of chart is the so-called "Gibson chart" which is represented in Chart I, the purpose of which is to show at a glance the ratio between the total white cell count and the polymorphonuclear percentage.

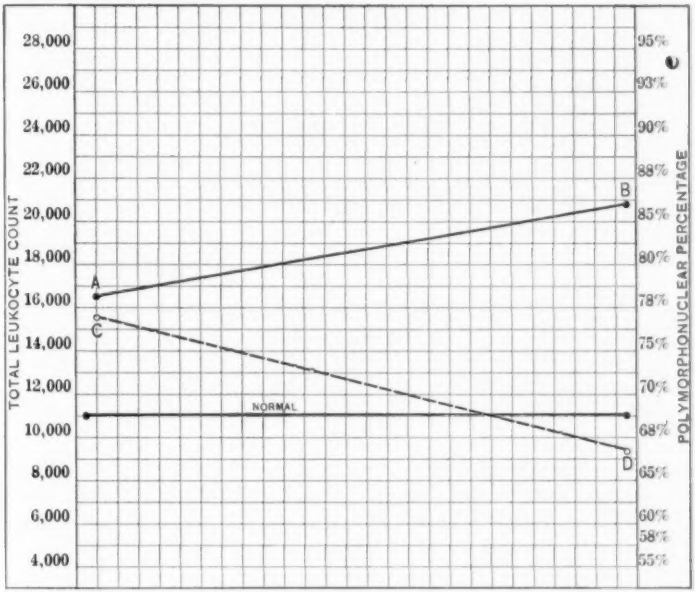


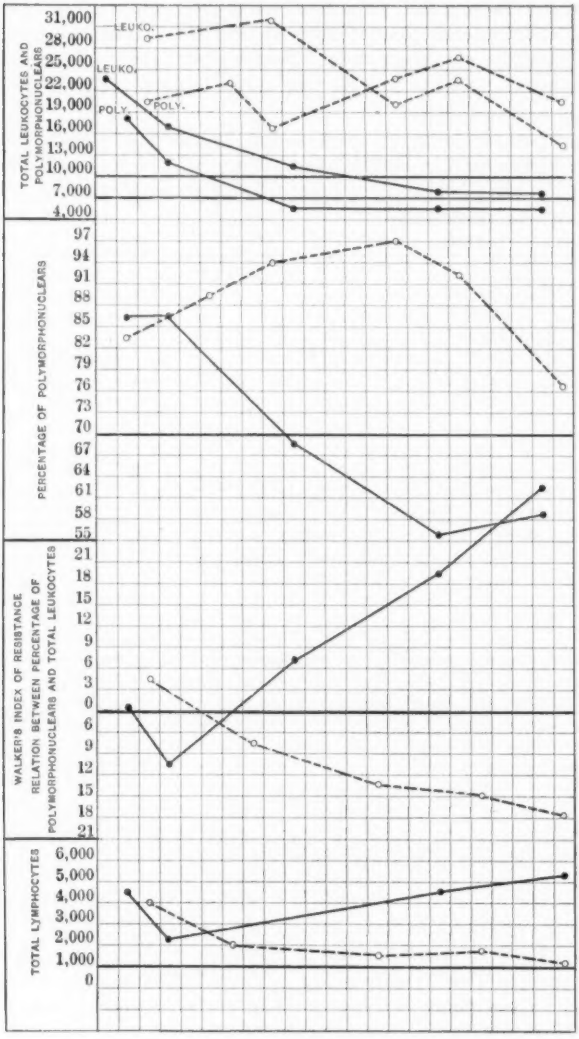
CHART I.—The Gibson chart.

The figures to the left of the chart indicate the total white cell count; those at the right hand margin the polymorphonuclear percentage. A line drawn from one to the other gives visual evidence of the degree to which the resisting powers of the patient are being utilized. In the chart the line A–B indicates a good resistance; the line C–D justifies an unfavorable inference.

Walker[11] has elaborated this conception somewhat and has com-

[11] An Index of Body Resistance in Acute Inflammatory Processes, Jour. Am. Med. Assn., 1919, **82**, 1453.

puted a very useful "index of body resistance." Taking 10,000 as the highest possible normal total white cell count, and 70 as the highest possible normal polymorphonuclear percentage, he assumes



Typical favorable findings: ●———●
Typical unfavorable findings: ○— - - - -○

CHART II.—Graphic blood count chart. (After Jones and Brown.)

that for every 1 per cent increase in the polymorphonuclear count there should be a corresponding rise in the total white cell count of 1000. For example, if the polymorphonuclear count is found to be 80 (10 above 70) the total white cell count should be 20,000 (10,000 above 10,000). The index in this case would be normal or zero, that is, no variation from the normal ratio. If, however, assuming a polymorphonuclear count of 80, the total white cell count were 25,000—or 5000 over and above the assumed ratio, then the index would be plus 5, and so on; if under the same circumstances the white cell count were only 15,000 with a polymorphonuclear count of 80, then the index lacking 5000 of the proportionate number expected, would be minus 5.

A positive or plus index is of favorable import; a negative index is, as a rule, unfavorable.

Jones and Brown have endeavored to combine all of this information in a single and very useful chart shown in Chart II. To make the chart the following data are required:

1. The total white cell count.
2. The polymorphonuclear percentage—obtained from the differ ential count.
3. The total number of polymorphonuclear cells: ascertained by multiplying the total count by the percentage of polymorphonuclears.
4. The total lymphocyte count per c.mm.: Obtained in the same manner.
5. Walker's index: Obtained as already described.

They describe the chart as follows: "The line in the upper portion of the figure opposite 10,000 represents the highest possible normal number of total leukocytes. The first line below this designates 7000 as the highest total number of polymorphonuclear cells. The line on a level with 70 designates the highest normal polymorphonuclear percentage. The line to the right from zero denotes normal resistance according to Walker's index. The lowest line on the right side indicates 1000 as the lowest possible normal number of lymphocytes per c.mm."

The vertical columns of arabic numerals are so arranged that exactly the same amount of space is allowed for a change of 1000 in the total leukocytes or total polymorphonuclears, for a variation of 1 per cent in the polymorphonuclears, and for a shifting of one point in Walker's index. The vertical columns under "total lymphocytes" have no definite relations as above described.

It seems that there should be a wide field of usefulness for such a graphic representation of blood counts as practically forcing the more accurate correlation and interpretation of the results obtained. Of course, as always, the interpretation is what gives a blood count any value and in this connection the following conclusions seem warranted:

1. Graphic representations of blood count findings are of more value than mere rows of figures and should be more widely resorted to.

2. The curve of a series of blood counts has more diagnostic and prognostic value than a single or isolated examination. A single enumeration, however, is not without some value when interpreted in the light of all the other data obtainable.

3. The total number of white cells is, in general, in proportion to the total polymorphonuclear count. Jones and Brown, however, emphasize that a divergence of these lines is most marked as the patient returns to normal while their convergence is a bad prognostic sign.

4. While a high polymorphonuclear percentage is indicative of severe infection, in the interpretation of a low polymorphonuclear percentage the general resisting powers of the patient must be taken into consideration; it may be an indication of the overwhelming force of the infection.

5. Walker's index, when normal, must be interpreted in the light of the features of other examinations made upon the patient; if the polymorphonuclear percentage is high, the normal index is of unfavorable import (Jones and Brown). The same workers report the observation that the total lymphocyte count parallels Walker's index.

Inferences based entirely upon numerical findings of the leukocyte count are not always to be relied upon and are best considered in the light of all the other clinical findings.

There has been a recent application of the leukocyte count to the diagnosis of hepatic conditions known as the crîse hemoclasique of Widal. While the method is of recent development, it promises to be of some value in the detection of hepatic lesions.

It is based upon the fact that the normal response to the ingestion of proteins is a leukocytosis which is held to be associated with the arrest or transformation by the liver of the peptones, proteosis, and other disintegrating substances of protein origin found in the portal vein during the digestive period. When by reason of various pathological changes the liver is deficient in this "proteopexic" function, the ingestion of proteins is followed by a leukopenia instead of a leukocytosis which constitutes the crîse hemoclasique.

The technic of the test is simple: After a five-hour fast—which is an essential preliminary—the total number of leukocytes is counted as usual and the patient given a glass (200 gm.) of milk. Leukocyte counts are then made every twenty minutes for two hours and the results charted. Normally, because of the ingestion of the protein, a slight leukocytosis occurs, usually within the first hour of the count, at all events does not drop below the original level. A leukopenia is taken as evidence of hepatic insufficiency. Other particulars of the reaction are a low blood-pressure, and an increased coagulation-time together with a decreased sero-refractive index; the leukopenia, however, is the most delicate sign and the easiest detected.

It is obvious, of course, that spontaneous variations in the leukocyte count are a possible source of error. Glaser and Buschman,[12] indeed, believe that this factor robs the test of much of its value, having found, in an examination of 333 patients, a spontaneous change in the count averaging 2000 per c.mm. in 55 per cent and even in 90 per cent if the counts were repeated on three days.

Feinblatt,[13] however, in a study of 80 normal subjects found that the normal response to the test was uniformly a leukocytosis and believes the test to be of value.

The exact nature of the reaction remains to be elucidated. Moutier and Rachet[14] found that the reaction—negative or positive—could be produced with the ingestion of distilled water as well as of milk and believe the crisis to be due to neurovascular reflexes which are independent of the chemical nature of the test substance.

Delbecq[15] believes that excitation of the pneumogastric nerve plays a part in the production of the hemoclastic crisis and that the rapidity with which the milk is ingested and the consequent degree of mechanical irritation, the temperature of the fluid, and the secretion of pepsin are all contributing factors.

The test is apparently giving consistent results though its exact status remains to be determined by future studies.

Summary. While the counting of blood cells and especially white blood cells is a most frequently utilized laboratory procedure, the correlation of the results with the clinical data is not attained to the fullest extent by reports which give simply the tabulated numerical findings. To call attention to this fact and to urge the greater usefulness of graphic methods of reporting these findings is the purpose of the present communication.

COMPOSITION AND PHYSICAL PROPERTIES OF NORMAL HUMAN BLOOD: A COMPILATION OF VALUES FROM THE LITERATURE.

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The chemical, physical and morphological examination of the blood every day gains more and more importance in practical and

[12] Spontaneous Variations in the Leukocyte Count, Med. Klin., 1923, **19**, 1143.

[13] Leukocytosis in Eighty Normal Men: A Study in Reference to the Crise Hemoclasique of Widal, Jour. Am. Med. Assn., 1923, **80**, 613.

[14] Hemoclastic Crises, Prog. méd., 469.

[15] Leukopenia in Shock, Paris méd., 1922, **13**, 218.

scientific medicine. It is impossible to peruse a medical periodical without coming upon statements of pathological values for one or more blood constituents. Even for the specialist in this subject it may be difficult to keep in mind the normal values required for a proper understanding of such findings. The necessary data are scattered in the fast growing literature, while the handbooks very often contain superannuated or false values. The following compilation of normal values was made for the author's own needs. It has proven so useful that it is felt worth while to make it available to others.

The values presented here have been chosen upon the following grounds. When possible, values obtained by modern methods on strictly normal subjects, not patients, have been chosen. Values which give or allow calculation of content in corpuscles and serum have been preferred to larger series on either whole blood or serum alone. Also series using both males and females have been preferred to observations on one sex only. Several sets of observations of the author have been introduced for one or other of these reasons and because of the uniformity in the manner of taking and handling of the blood.

In the following tables the maximum, minimum and average are generally given, where such are available. Sometimes, however, only the average is recorded, when the observations are too few to give any idea of the possible variations. A differentiation between men and women is generally made only where an acknowledged sex difference is present or in some cases because the tables quoted were so arranged.

I. The Ordinary and Morphological Blood Examination. Hemoglobin, erythrocytes, differential leukocytes, count, the Arneth blood picture, reticulated erythrocytes, cell volume, diameter of erythrocytes, color index, volume index, ratio $\frac{\text{hemoglobin}}{\text{cell vol. per cent}}$

TABLE I.—HEMOGLOBIN PER CENT.

100 per cent = 18.5 volume per cent oxygen capacity = 13.8 gm. hemoglobin per 100 cc.)

	Bie and Moeller.[1] (Meisling colorimeter standardized by gas pump oxygen determinations.)				Gram and Norgaard.[2] (Autenrieth colorimeter standardized by Van Slyke oxygen determinations.)			
	Men.		Women.		Men.		Women.	
	Per cent.	Gm. per 100 cc.	Per cent.	Gm. per 100 cc.	Per cent.	Gm. per 100 cc.	Per cent.	Gm. per 100 cc.
Maximum . .	120	16.6	101	13.9	118	16.3	102	14.1
Minimum . .	99	13.7	89	12.3	96	13.2	88	12.1
Average . . .	107	14.8	96	13.2	109	15.0	94	13.0
Subjects . . .	10	...	10	...	10	...	10	

TABLE II.—ERYTHROCYTES: MILLIONS PER 1 C.MM. BLOOD.

	Bie and Moeller.[1]		Gram and Norgaard.[2]		Gram.[3]	
	Men.	Women.	Men.	Women.	Men.	Women.
Maximum	**6.395**	5.21	5.91	5.05	5.82	**5.33**
Minimum	4.99	4.25	**4.85**	4.36	4.85	**4.21**
Average	5.53	4.74	5.45	4.65	5.37	4.78
Subjects	10	10	10	10	32	56

TABLE III.—LEUKOCYTES PER 1 C.MM.

	Men.	Women.
Maximum	9200	10300
Minimum	4400	4600
Average	6300	7200
Subjects	25	24

The values are very labile. Data in table refer to venous blood of fasting normal individuals.[4]

TABLE IV.—DIFFERENTIAL COUNT IN PER CENT OF TOTAL LEUKOCYTES.

	Naegeli.[5]	Pappenheim.[6]
Lymphocytes	22–25	23
Monocytes	3–5	2–6
Neutrophiles	65–70	65–72
Eosinophiles	2–4	2–4
Basophiles	0.5	0.5

The number of subjects are not given.

TABLE V.—THE ARNETH BLOOD PICTURE.

(Number of nuclear segments in neutrophile leukocytes.)

1 segment	2 segments	3 segments	4 segments	5 or more segments
5 per cent	35 per cent	41 per cent	17 per cent	2 per cent

Number of subjects are not quoted.[7 8]

TABLE VI.—PERCENTAGE OF RETICULATED ERYTHROCYTES.

Less than 1 per cent.[9 10]

TABLE VII.—CELL VOLUME PERCENTAGE.*

	Gram and Norgaard[2] (Hirudin-blood, hematokrit).		Gram[11 12] (Citrated blood, larger tubes).	
	Men.	Women.	Men.	Women.†
Maximum	50.0	43.0	51	45
Minimum	42.4	38.8	43	36
Average	46.3	40.6	48	40
Subjects	10	10	25	96

* According to Gram and Norgaard's figures for the cell count, the average volume of a normal erythrocyte would be 85.9 μ^3.

† Combination of two series by same technic.

The cell volume is altered slightly by changes of reaction.

If the cell volume at pH 7.4 is called 100 it will be 104 at pH 7.8 and 96 at pH 7.0. (Warburg.[13])

TABLE VIII.—DIAMETER OF THE ERYTHROCYTES (MEASURED IN THEIR OWN SERUM.)

Mean diameter[14 15]	Maximum	8.0 μ
	Minimum	7.7 μ
	Average	7.8 μ
Greatest diameter of single erythrocyte		9 μ
Smallest diameter of single erythrocyte		6 μ

TABLE IX.—COLOR INDEX.

(Calculated with 100 per cent Hemoglobin = 18.5 per cent oxygen capacity.)

$$\text{Formula: Index} = \frac{\text{Hemoglobin, per cent}}{\text{Millions of cells per c.mm.} \times 20}$$

Maximum[2]	1.05
Minimum	0.98
Average	1.00
Subjects	20

There is no appreciable sex variation. The normal deviation from 1.00 depends mainly on the precision of the methods employed. With ordinary clinical precision values between 0.9 and 1.1 can be considered as normal.

TABLE X.—VOLUME INDEX.

(Calculated assuming 5,000,000 normal cells per c.mm. = 42.96 volume per cent.)

$$\text{Formula: V.I.} = \frac{\text{Volume per cent} \times 0.1164}{\text{Millions of erythrocytes per c.mm.}}$$

Maximum[2]	1.06
Minimum	0.96
Average	1.00
Subjects	20

TABLE XI.

$$\text{Ratio} \frac{\text{Hemoglobin, per cent}}{\text{Volume per cent}}$$

Maximum[2]	2.47
Minimum	2.24
Average	2.34
Subjects	20

II. Facts Pertaining to Coagulation and Hemostasis. Platelet count, clotting-time and bleeding-time.

TABLE XII.—BLOOD PLATELETS PER 1 C.MM. BLOOD.

Maximum	540,000
Minimum	280,000
Average around	350,000
Subjects	25

These figures[16] refer to venous blood by Oluf Thomsen's technic. When skin blood is used the figures tend to be lower and are much less reliable.

Coagulation-time. The coagulation-time of blood depends very much on technic and handling and whether the end-point chosen is the first appearance of fibrin or the solid clotting. A simultaneous control with normal blood should be done.

1. The more contact, the quicker the coagulation.
2. The higher temperature, the quicker the coagulation.
3. Blood from skin cuts clots quicker than venous blood.

The following values are for venous blood in test-tubes.

TABLE XIII.—COAGULATION-TIME.

Normal values min.	Stage of coagulation taken as end-point.	Characteristics of method.	Temperature, °C.	Author.
Average 6½	Middle	Immobility of surface of 1 cc blood in test-tube	37	Lee and White.[17]
3 to 8	Middle	Immobility of surface of 1 cc blood in test-tube	35	Gram.[18]
Average 2	Beginning	Adhesion of fibrin to wire loop moved in 20 cc blood kept in test-tube	37	Bachrach and Tittinger.[19]

TABLE XIV.—BLEEDING-TIME. (DUKE.)

Maximum[16]	4	minutes
Minimum	1½	"
Subjects	100	

III. Arterial and Venous Blood.

TABLE XV.—SYNOPSIS OF DIFFERENCE BETWEEN ARTERIAL AND VENOUS BLOOD.[20]

	Arterial.	Venous.
pH* (plasma)	7.30 to 7.40	7.27 to 7.37
Free CO_2 (blood)†	1.5 to 4.0 vol. per cent (0.67 to 1.8 m-M per L.)	1.7 to 4.2 vol. per cent. (0.76 to 1.87 m-M per L.)
Bound CO_2† or $BHCO_3$ (blood)	31 to 56 vol. per cent (14 to 25 m-M per L.)	36 to 61 vol. per cent. (16 to 27 m-M per L.)
Plasma-Cl‡ (as NaCl)	0.614 to 0.642 gm. per 100 cc (105 to 110 m-M per L.)	0.596 to 0.625 gm. per 100 cc. (102 to 107 m-M per L.)
Percentile oxygen** saturation of hemoglobin	93 to 98 per cent	62 to 85 per cent.
Oxygen** content	17 to 22 vol. per cent (7.6 to 9.8 m-M per L.)	11 to 16 vol. per cent. (4.9 to 7.0 m-M per L.)

* See also Table XXX.
† See also Table XIX.
‡ See also Table XXVI.
** See also Table XVII.

IV. Gases of the Blood. Oxygen capacity, oxygen content and unsaturation, total CO_2, free and bound CO_2.

TABLE XVI.—OXYGEN CAPACITY (= VOLUME PER CENT OXYGEN REDUCED TO 0° C. AND 760 MM. HG. BOUND BY 100 CC OF BLOOD).

(Calculated by Gram and Norgaard and Bie and Moeller's colorimetric data. Formula: 18.5 volume per cent O_2 = 100 per cent hemoglobin. See Table I of hemoglobin.)

	Bie and Moeller.[1]		Gram and Norgaard.[2]	
	Men.	Women.	Men.	Women.
Maximum	22.2	18.7	21.8	18.9
Minimum	18.3	16.5	17.8	16.1
Average	19.8	17.8	20.2	17.4
Subjects	10	10	10	10

TABLE XVII.—OXYGEN CONTENT AND OXYGEN UNSATURATION OF VENOUS BLOOD OF MALES* (VAN SLYKE TECHNIC).

	Oxygen content, vol. per cent.	Oxygen unsaturation, vol. per cent.†
Maximum[21]	17.98	8.95
Minimum	9.55	2.70
Average	13.60	5.80
Subjects	12	12

* See also Table XV of differences between arterial and venous blood.
† Oxygen unsaturation = oxygen capacity − oxygen content.

Dissolved oxygen and nitrogen (reduced):

	Vol. per cent.
Blood saturated with air at room temperature	2.11
Arterial blood	1.70
Venous blood	1.50

TABLE XVIII.—TOTAL CO_2 OF VENOUS OXALATED PLASMA AND BLOOD OF MALES* (VAN SLYKE TECHNIC).

	Plasma.		Blood.	
	Volume per cent.	Millimol per L.	Volume per cent.	Millimol per L.
Maximum[22]	70.8	31.6	61.2	27.3
Minimum	59.6	26.6	52.0	23.2
Average	67.7	30.2	57.4	25.6
Subjects	14		23	

$$\text{Millimols } CO_2 \text{ per L.} = \frac{\text{Volume per cent } CO_2}{2.24\dagger}$$

* See also Table XV of differences between arterial and venous blood.
† According to Warburg 2.2263 for CO_2. Biochem. Jour., 1922, **16**, 11.

TABLE XIX.—FREE AND BOUND CO_2 OF VENOUS PLASMA.

(Calculated from data of Cullen and Robinson by Hasselbalch's equation:

$$[pH = pK_1 + \log \frac{BHCO_3}{H_2CO_3}] \text{ with } pK_1 = 6.1)$$

	Plasma, m-M per L.	
	H_2CO_3.	$BHCO_3$.
Maximum	1.9	30.2
Minimum	1.3	26.4
Average	1.6	28.6
Subjects	14	

V. Various Substances in Serum (Plasma), Corpuscles and Whole Blood. Inorganic constituents of serum, inorganic constituents of corpuscles, inorganic constituents of blood, acid-base composition of venous plasma, phosphoric acid compounds and inorganic phosphorus, lactic acid, chloride, non-protein nitrogen, total nitrogen, hydrogen-ion concentration, bile pigment and plasma color, sugar, dry substance, serum proteins, ratio $\frac{\text{albumin}}{\text{globulin}}$, fibrin.

TABLE XX.—CONTENT OF INORGANIC SUBSTANCES IN SERUM (PLASMA).*

	Milligrams per 100 cc.	Millimols per L.	Subjects.	Author.
Cl†	357–381	100.60–107.60	10	Gram, H.-C.[23]
S	0.5–0.9	0.16– 0.28	10	Denis, W., and Hobson, S.[24]
P‡ (inorg.)	3.2–4.3	1.03– 1.39	22	Tisdall, F.[25]
K	18–21	4.60– 5.40	26	Kramer, B., and Tisdall, F.[26]
Na	326–350	141.70–152.20	18	Kramer, B., and Tisdall, F.
Ca	9–11	2.25– 2.75	8	Halverson, Mohler and Bergein.[28]
Mg	2.2–3.5	0.91– 1.40	?	Marriott, W. McK. and Howland, J.[29]
NH_4 (calculated as NH_3)	0.14–0.3	0.01– 0.02	6	Morgulis, S., and Jahr, H. M.[30]

* Values recalculated into milligrams per 100 cc and millimols per L. Chlorides, phosphates and sulphates stated as Cl, P and S.

† See, however, Table XXVI of chlorides concerning the influence of the CO_2 content.

‡ Compare the lower values to be calculated from Bloor's result in Table XXIIIa of phosphoric acid compounds.

TABLE XXI.—AVERAGE CONTENT OF INORGANIC SUBSTANCES IN THE CORPUSCLES.*

	Milligrams per 100 cc.	Millimols per L.	Subjects.	Author.
Cl†	186	52.50	22 (27 obs.)	Gram, H. C., and Norgaard, A.[31]
S (inorg.):	Nearly same content as that of serum.		See Tables XX and XXII.	
P (inorg.)	5.44	1.75	27	Bloor, W. R.[32]
K	425	109.00	..	See footnote ‡.
Na	43	18.80	1	Schmidt, C.; quoted by Matthews, A. P.[33]
Ca	3.47	0.87	1	Cowie, D. M., and Calhoun, H. A.[34]
Mg.	Nearly same content as that of serum.		See Tables XX and XXII.	

* Some of these values are uncertain, being based on few determinations or somewhat doubtful calculations.

† See, however, Table XXVI of chlorides concerning the influence of the CO_2 content.

‡ K content calculated by using the average figures in two series by Kramer and Tisdall: K serum, 19.7 mg. per 100 cc; K blood, 182 mg. per 100 cc, with an average cell volume of 40 per cent. The corresponding calculation for sodium, however, gives a negative value, wherefore Schmidt's single determination has been used.

TABLE XXII.—CONTENT OF INORGANIC SUBSTANCES IN WHOLE BLOOD.

	Milligrams per cc.	Millimols per L.	Subjects.	Author.
Cl	273–321	77.00–90.60	15	Gram, H. C., and Norgaard, A.[31]
S (inorg.)	0.5–1.1	0.16– 0.34	10	Denis, W.[36]
P (inorg.):	Between values for serum and corpuscles.			See Tables XX and XXI.
K	153–201	39.20–51.60	13	Kramer, B., and Tisdall, F.[36]
Na	170–225	73.90–97.80	6	Kramer, B., and Tisdall, F.[37]
Ca	5.3–6.8	1.30– 1.70	13	Kramer, B., and Tisdall, F.[38]
Mg	2.3–4.0	0.90– 1.60	8	Kramer, B., and Tisdall, F.[39]

Values more variable than those for serum and corpuscles on account of the uneven distribution and different cell volumes.

TABLE XXIII*a*.—PHOSPHORIC ACID COMPOUNDS IN PLASMA AND CORPUSCLES (BLOOR).

Milligrams H_3PO_4 per 100 cc.[41]

(To transform into P use equation: $P = 0.316\ H_3PO_4$.)

Men.	Plasma.					Corpuscles.				
	Total.	Acid soluble.	Inorg.	Lipoid.	Other forms.	Total.	Acid soluble.	Inorg.	Lipoid.	Other forms.
Men:										
Maximum	43.5	13.7	12.0	23.3	4.00	325.0	250.0	27.3	66.6	238.0
Minimum	24.3	7.5	6.0	16.0	0.40	185.0	140.0	12.0	43.5	123.0
Average	32.0	10.4	8.7	22.1	1.70	248.0	188.0	18.7	57.0	172.0
Subjects	17					17				
Women:										
Maximum	41.0	14.3	13.8	29.0	4.00	265.0	206.0	26.3	62.5	188.3
Minimum	31.0	9.4	8.0	19.0	0.00	218.0	160.0	9.8	47.0	133.7
Average	36.2	12.4	11.2	24.9	1.26	249.0	187.0	15.7	56.6	167.0
Subjects	10					10				

Definitions of fractions:

1. Acid-soluble: Soluble in dilute acids and precipitated with the proteins by alcohol-ether.

2. Lipoid: Soluble in alcohol-ether and precipitated with the proteins by dilute acids.

3. In the first group are included inorganic phosphorus and an unknown compound; in the second substances of the type of lecithin.

TABLE XXIII*b*.—INORGANIC PHOSPHORUS IN SERUM* (TISDALL'S TECHNIC).

	Milligrams of P per 100 cc.[42]
Maximum	4.3
Minimum	3.2
Average	3.8
Subjects	22

* Higher values 6.4 to 4.6, average 5.4 mg. per 100 cc in serum of children.

TABLE XXIV.—AVERAGE ACID-BASE COMPOSITION OF VENOUS PLASMA.[40]

	Cations, milliequivalents per L.		Anions, milliequivalents per L.
Na	143.4	HCO_3	27.0
K	5.1	Cl	103.0
Ca	5.0	HPO_4	3.0
Mg	2.5	SO_4	1.0
		Organic acids	2.0
		Proteins*	20.0
Sum	156.0	Sum	156.0

* Calculated by differences.

The ammonium value is too small to be considered. The values in grams or millimols can be calculated from atomic weight and valency.

Atomic weights: H 1, Na 23, K 39, Ca 40, Mg. 24, C 12, O 16, N 14, P 31, S 32, Cl 35.5.

Physiological valency: Ca 2, Mg. 2, SO_4 2, HPO_4 1.8.

1 gm. molecule = 1000 millimols.

Millimols × valency = milliequivalents = cc of 0.1 normal per 100 cc.

TABLE XXV.—LACTIC ACID IN WHOLE BLOOD OF CHILDREN (CLAUSEN TECHNIC).

	Milligrams per 100 cc.[43]	Millimols per L.
Maximum	35	3.9
Minimum	18	2.0
Average	25	2.8

Number of subjects not given.

TABLE XXVI.—CHLORIDE *as NaCl* IN SERUM OR PLASMA.

(From whole blood exposed to air with loss of CO_2.)

	Gram[23] (modified Austin and Van Slyke technic).		Gram and Norgaard[44] (modified Bang technic).	
	Milligrams per 100 cc serum.	Millimols per L. serum.	Milligrams per 100 cc hirudin plasma.	Millimols per L. hirudin plasma.
Maximum	629	107.6	625	106.9
Minimum	588	100.6	595	101.8
Average	604	103.3	613	104.9
Subjects	10	...	7	

(12 determinations)

The chloride content of the whole blood depends largely on the cell volume, as the cells contain only approximately half as much Cl as the serum. The distribution between serum and cell changes with the variation in the CO_2 content of the blood, so that the concentration of Cl of serum decreases with increasing CO_2 content (see Table XV of differences between arterial and venous blood). In 15 presumably normal persons Gram and Norgaard[31] found on the average, 0.31 per cent, calculated as NaCl, in the corpuscles; a later series of 12 determinations on 7 strictly normal persons gave an average of 0.304 per cent NaCl. On whole blood (cell volume 40 to 50 per cent) the same authors found 0.45 to 0.53 per cent NaCl, while Gettler and Baker[45] found from 0.4 to 0.531 per cent.

TABLE XXVII.—LIPOIDS IN WHOLE BLOOD, PLASMA AND CORPUSCLES (BLOOR TECHNIC).

Averages in grams per 100 cc.[46]

	Men.	Women.
Total fatty acids:		
Blood	0.36	0.36
Plasma	0.38	0.40
Corpuscles	0.35	0.29
Lecithin:		
Blood	0.30	0.29
Plasma	0.22	0.19
Corpuscles	0.40	0.44
Cholesterin:		
Blood	0.21	0.23
Plasma	0.22	0.24
Corpuscles	0.19	0.21
Fat:		
Plasma	0.14	0.16
Corpuscles	0.07	0.00
Total lipoids:		
Plasma	0.67	0.69

Number of subjects not given.

TABLE XXVIII*a*.—NON-PROTEIN NITROGEN AND ITS FRACTIONS IN BLOOD, PLASMA AND CORPUSCLES.

Milligrams N. per 100 cc. of blood.[47]

	Maximum.	Minimum.	Average.
Blood:			
Amino-acid N.	7.8	5.7	6.4
Urea N.*	15.2	8.9	11.5
Undetermined N	17.5	10.1	13.7
Total non-protein N.	**39.4**	**27.8**	**32.1**
Plasma:			
Amino-acid N.	6.2	4.3	5.3
Urea N.*	17.3	9.6	12.4
Undetermined N	11.5	1.8	6.7
Total non-protein N.	**30.0**	**18.0**	**24.7**
Corpuscles:			
Amino-acid N.	10.7	6.7	8.2
Urea N.*	13.2	7.7	10.3
Undetermined N.	33.8	18.3	24.7
Total non-protein N.	**55.0**	**37.7**	**43.6**

Subjects, 12

* To transform into milligrams urea use equation: Urea = 2.125 urea N.

TABLE XVIII*b*.—QUANTITIES OF SOME OTHER NITROGEN-CONTAINING CONSTITUENTS IN THE WHOLE BLOOD.[48]

	Milligrams per 100 cc. of blood.
Uric acid	0.7–3.0
Creatinin	1.2–1.5
Creatin (mainly in corpuscles)	3.5–5.0

Number of subjects not given.

TABLE XXIX.—TOTAL NITROGEN OF SERUM AND BLOOD.

	Serum.*	Blood,† gm. per 100 cc.
Maximum[45]	1.43	4.10
Minimum	1.20	3.00
Average	1.31	3.43
Subjects	30	30

* Plasma should show slightly higher figures by as much as $\frac{\text{Fibrin per cent}}{6.25}$ See Table XXXVI of fibrin content of plasma.

† The total N. of blood depends partly on cell volume as the corpuscles contain more protein and also more non-protein nitrogen than the serum.

TABLE XXX.—HYDROGEN-ION CONCENTRATION (EXPRESSED AS pH) IN VENOUS OXALATED PLASMA OF MEN.*

	pH.
Maximum[22]	7.41
Minimum	7.28
Average	7.36
Subjects	27

* Precautions against loss of CO_2. Colorimetric determination of Cullen corrected to pH electrometric at 38° C.

The corpuscles are somewhat more acid (that is, pH is 0.10 to 0.15 smaller). Arterial plasma is about 0.03 pH more alkaline. See Table XV of differences between arterial and venous blood.

TABLE XXXI*a*.—PLASMA COLOR.

(Meulengracht[9] plasma color: Volume of 1 cc plasma diluted to equality of color with a chromic standard color.)

Men	1 to 5
Women	1 to 3

Subjects: 34 men and 40 women.

TABLE XXXI*b*.—BILE PIGMENT OF SERUM.

(Bilirubin units of van den Bergh[49] = 1 unit = 0.5 mg. in 100 cc.)
Normal = 0.5 to 1 unit.

TABLE XXXII.—SUGAR (DEXTROSE) IN BLOOD, PLASMA AND CORPUSCLES. (FASTING INDIVIDUAL. HAGEDORN TECHNIC.)

	Milligrams per 100 cc.*		
	Blood.	Plasma.	Corpuscles.
Maximum[50]	116	114	121
Minimum	79	77	77
Average	99	98	100
Subjects	28	28	28

* To transform into m-M per L. use equation: m-M per L. = 0.0556 × mg. per 100 cc.

After the meals the values are much more variable.

TABLE XXXIII.—DRY SUBSTANCE OF SERUM, BLOOD AND CORPUSCLES.[1]

	Serum, gm. per 100 gm.		Blood, gm. per 100 gm.		Corpuscles, gm. per 100 gm.	
	Men.	Women.	Men.	Women.	Men.	Women.
Maximum	9.750	9.395	21.820	19.755	35.730	36.630
Minimum	8.555	8.400	19.915	18.010	33.100	33.470
Average	9.010	8.770	20.890	18.990	34.606	35.193
Subjects	10	10	10	10	10	10

To convert into grams per 100 cc multiply by average specific gravities in Table XLI.

TABLE XXXIV.—TOTAL SERUM PROTEINS.

	Gram[23] (refractometric), gm. per 100 cc.	Gettler[45] (from nitrogen),* gm. per 100 cc.	Atchley.[51] (refractometric), gm. per 100 cc.	Atchley.[51] (from nitrogen), gm. per 100 cc.
Maximum	8.8	8.7	8.5	8.1
Minimum	7.7	7.3	7.4	7.2
Average	8.05	8.0	8.0	7.5
Subjects	10	30	18†	18‡

* Calculated from these authors total nitrogen figures, subtracting the average non-protein nitrogen of serum and multiplying by 6.25. See Tables XXVIII*a* and XXIX of non-protein nitrogen and total nitrogen.

† 28 determinations. ‡ 26 determinations.

TABLE XXXV.—RATIO $\frac{\text{ALBUMIN}}{\text{GLOBULIN}}$ OF SERUM.

	Alder[43] (Rohrer's technic).	Linder[53] (Howe's technic).
Maximum	4.0	2.0
Minimum	1.2	1.2
Average	..	1.6
Subjects	62	12

TABLE XXXVI.—FIBRIN IN PLASMA AND BLOOD (GRAM'S TECHNIC).[11]

	Plasma, gm. per 100 cc.		Blood, gm. per 100 cc.	
	Men.	Women.	Men.	Women.
Maximum	0.36	0.38	0.19	0.21
Minimum	0.20	0.21	0.11	0.12
Average	0.27	0.29	0.14	0.17
Subjects	25	25	25	25

The percentage per 100 cc blood depends to a large extent on the cell volume.

VI. Some Physical Properties of Blood and its Constituents. Resistance of corpuscles to hypotonic salt solutions, sedimentation of corpuscles, freezing-point depression of serum, conductivity and corrected conductivity of serum, specific gravity of serum and corpuscles, viscosity of serum and blood, refractive index of serum.

TABLE XXXVII.—RESISTANCE AGAINST HYPOTONIC SALT SOLUTIONS.

(1 drop corpuscles in 2 cc solution.[15])

	NaCl, per cent.
Beginning hemolysis	0.48–0.42
Half hemolysis	0.42–0.38
Total hemolysis	0.38–0.32
Subjects	20

TABLE XXXVIII.—SEDIMENTATION OF THE CORPUSCLES.

(Measured by the height of the plasma layer.)

	Gram[54] (Blood column 50 mm. high, 1 part 3 per cent Na citrate and 9 parts blood.) After one hour.		Fåhraeus[55] (Blood column 150 mm. high, 1 part 2 per cent Na citrate and 4 parts blood.) After one hour.	
	Men. mm.	Women. mm.	Men. mm.	Women mm.
Maximum	5	13	9.0	29.0
Minimum	Less than 1	2	0.5	2.0
Average	Less than 2	6	3.3	7.4
Subjects	10	10	82	61

TABLE XXXIX.—FREEZING-POINT DEPRESSION ($\triangle$) OF SERUM AND ITS EQUIVALENTS IN NaCl AND NON-DISSOCIATED CRYSTALLOIDS.

		NaCl equivalent.[56]		Equivalent of non-dissociated crystalloids,*
	$\triangle$ – ° C.	Grams per 100 cc.	Millimol per L.	Millimols per L.
Maximum[23]	0.570	0.972	164.6	308.1
Minimum	0.555	0.946	161.8	300.0
Average	0.562	0.958	163.9	303.8

* Depression caused by 1 gram-molecule per L. = 1.85° C.

The osmotic pressure in the cells is the same as that of the serum

TABLE XL*a*.—ELECTRICAL CONDUCTIVITY OF SERUM AT 20° C. AND 25° C.*

	Gram[22] (ionometer).			Atchley[21] (bridge), $K_{25°} \times 10^4$.
	$K_{20°} \times 10^4$.	NaCl equivalent. Grams per 100 cc.	NaCl equivalent. Millimols per L.	
Maximum	111.0	0.674	115.3	123.9
Minimum	104.8	0.640	109.5	116.5
Average	106.3	0.652	111.6	119.9
Subjects	30			18†

* Correction of NaCl equivalent for temperature between 15° and 25° is approximately +2.06 per cent for each degree rise of temperature.

† 28 determinations.

The conductivity of blood depends[57] on the cell volume. The ratio $\frac{\text{conductivity of serum}}{\text{conductivity of blood}}$ is a constant for each cell volume. These constants are 2.07 for 38 vol. per cent, 2.39 for 44 vol. per cent and 2.8 for 50 vol. per cent.[58]

TABLE XL*b*.—SERUM CONDUCTIVITY AT 20° C. CORRECTED FOR DEPRESSING INFLUENCE OF PROTEINS.

(Formula:[59] Corr. conduct. = obs. conduct. $\times \frac{100}{100 - (2.2 \times \text{protein per cent})}$

	Corrected NaCl equivalent.	
	Grams per 100 cc.	Millimols per L.
Maximum	0.811	138.8
Minimum	0.787	134.6
Average	0.799	136.7
Subjects	10	

TABLE XLI.—SPECIFIC GRAVITY OF SERUM AND CORPUSCLES AT 20° C.

	Serum (Gettler[60]).	Corpuscles (Schmidt[60]).
Maximum	1.0380	1.0889
Minimum	1.0241	1.0880
Average	1.0293	1.0885
Subjects	30	Not given.

The specific gravity of whole blood will depend mainly on cell volume and specific gravity of serum (average 1.05 to 1.06).

TABLE XLII.—VISCOSITY OF SERUM AND BLOOD.

(Hess viscosimeter at 20° C.)

	Serum.	Blood.
Maximum[61]	1.7	5.4
Minimum	2.0	3.6

Number of subjects not given.

Correction for temperature is +0.8 per cent for each degree increase of temperature between 15 and 25° C.

TABLE XLIII.—REFRACTIVE INDEX OF SERUM AT 17.5° C.

(Abbé refractometer, refractive index of distilled water being 1.33320.)

Maximum[62]	1.35110
Minimum	1.34920
Subjects	12

VII. Total Volume.

TABLE XLIV*a*.—TOTAL BLOOD AND SERUM VOLUME (VITAL-RED METHOD).

	Plasma.		Total blood.	
	Volume, cc.	Cc per 100 gm. body weight.	Volume, cc.	Cc. per 100 gm. body weight.
Maximum[63]	3750	5.8	6675	10.4
Minimum	250	4.3	4200	8.2
Average	3033	5.[illegible]	5447	9.0
Subjects	24		18	

Body weight: Plasma, 74 to 51 kg.; total blood, 85 to 47 kg.

TABLE XLIV*b*.—BLOOD VOLUME (CO METHOD).

	Total volume, cc.	Cc per 100 gm. body weight.
Maximum[64]	4601	6.99
Minimum	3429	5.23
Average	3888	5.95
Subjects	6 (7 determinations)	

Body weight: 72.7 to 60.9 kg.

The discrepancy in blood volume between the results of the dye and the CO methods is mainly due to the fact that the first measures a substance in the serum from which the blood volume is calculated; the second, a substance in the cells. A combination of the two methods would give better results, eliminating the influence of a varied $\frac{\text{serum}}{\text{corpuscle}}$ ratio in the different vascular areas.[65]

Summary. Forty-four tables are presented, giving the normal figures for various chemical, physical and morphological examinations of the blood.

BIBLIOGRAPHY:

1. Bie, V., and Moeller, P.: Arch. d. mal. d. cœur., 1922, **15**, 177.
2. Gram, H. C., and Norgaard, A.: Arch. Int. Med., 1923, **31**, 364.
3. Gram, H. C.: Ugesk. f. Læger., 1920, **82**, 1543.
4. Gram, H. C.: Studier over fibrin-maengden, Copenhagen, 1921, Thesis.
5. Naegeli, O.: Blutkrankheiten und Blutdiagnostik, Leipzig, 1908.
6. Pappenheim, A.: Les leucocytes à l'état normal, Traité du sang., Paris, 1913, **1**, 259.
7. Arneth: Die neutrof. weissen Blutkoerperchen bei Infektionskrankheiten, Jena, 1904.
8. Arneth: Die qualitative Blutlehre, Leipzig, 1920.
9. Meulengracht, E.: Der chronische, hereditäre, hämolytische Ikterus, Leipzig, 1922.
10. Chauffard, A., and Fiessinger, N.: Bull. et mém. Soc. méd. d. hop. d. Paris, 1907, **24**, 1169.
11. Gram, H. C.: Acta med., Scandinavica, 1922, **56**, 107.
12. Gram, H. C.: Ugesk. f. Læger., 1920, **82**, 1609.
13. Warburg, E.: Biochem. Jour., 1922, **16**, 133.
14. Gram, C.: Thesis, Copenhagen, 1883.
15. Meulengracht, E.: Der chronische hereditäre, hämolytische Ikterus, Leipzig, 1922.
16. Gram, H. C.: Arch. Int. Med. (this paper gives the limits 200,000 to 550,000 on a larger number of not strictly normal persons), 1920, **25**, 325.
17. Lee and White: Am. Jour. Med. Sci., 1913, **145**, 495.
18. Gram, H. C.: Bull. Johns Hopkins Hosp., 1920, **31**, 363.
19. Bachrach and Tittinger: Wien. klin. Wchnschr., 1910, 394.
20. Wilson, D. W.: Physiol. Rev., 1923, **3**, 295.
21. Lundsgaard, C.: Jour. Biol. Chem., 1918, **33**, 133.
22. Cullen, G. E., and Robinson, H.: Jour. Biol. Chem., 1923, **57**, 533.
23. Gram, H. C.: Jour. Biol. Chem., 1923, **56**, 593.
24. Denis, W., and Hobson, S.: Jour. Biol. Chem., 1923, **55**, 183.
25. Tisdall, F.: Jour. Biol. Chem., 1922, **1**, 329.
26. Kramer, B., and Tisdall, F.: Jour. Biol. Chem., 1921, **46**, 348.
27. Kramer, B., and Tisdall, F.: Jour. Biol. Chem., 1921, **46**, 467.
28. Halverson, Mohler and Bergein: Jour. Biol. Chem., 1917, **32**, 171.
29. Marriott, W., McK., and Howland, J.: Jour. Biol. Chem., 1917, **32**, 233.
30. Morgulis, S., and Jahr., H. M.: Jour. Biol. Chem., 1919, **38**, 435.
31. Gram, H. C., and Norgaard, A.: Jour. Biol. Chem., 1921, **49**, 264; 1923, **56**, 429.

32. Bloor, W. R.: Jour. Biol. Chem., 1918, **36**, 49.
33. Schmidt, C., quoted by A. P. Matthews: Physiol. Chem., 1915, New York.
34. Cowie, D. M., and Calhoun, H. A.: Jour. Biol. Chem., 1919, **37**, 505.
35. Denis, W.: Jour. Biol. Chem., 1921, **49**, 311.
36. Kramer, B., and Tisdall, F.: Jour. Biol. Chem., 1921, **48**, 223.
37. Ibid.
38. Ibid.
39. Ibid.
40. Gamble, Ross and Tisdall: Jour. Biol. Chem., 1923, **57**, 635.
41. Bloor, W. R.: Jour. Biol. Chem., 1918, **36**, 49.
42. Tisdall, F.: Jour. Biol. Chem., 1922, **50**, 329.
43. Clausen, S. W.: Jour. Biol. Chem., 1921, **46**, xviii.
44. Gram, H. C., and Norgaard, A.: Jour. Biol. Chem., 1923, **56**, 429.
45. Gettler, A. O., and Baker, W.: Jour. Biol. Chem., 1916, **25**, 211.
46. Bloor, W. R., and McPherson, D.: Jour. Biol. Chem., 1917, **31**, 79.
47. Folin, O., and Berglund, H.: Jour. Biol. Chem., 1922, **51**, 415.
48. Folin, O.: Physiol. Rev., 1922, **2**, 460.
49. van den Bergh, H.: Der Gallenfarbstoff im Blute, Leipzig, 1918.
50. Hansen, K. M.: Acta. med. Scandin., 1923, Suppl., 1.
51. Atchley, D. W., Loeb, R. F., Benedict, E. M., and Palmer, W. W.: Arch. Int. Med., 1923, **31**, 606.
52. Alder, A.: Deutsch. Arch. f. klin. Med., 1918, **126**, 61.
53. Linder, G. C., Lundsgaard, C., and Van Slyke, D. D.: Unpublished figures quoted by Salvesen, H., and Linder, G. C.: Jour. Biol. Chem., 1923, **58**, 617.
54. Gram, H. C.: Arch. Int. Med., 1921, **28**, 312.
55. Fåhraeus, R.: Acta. med. Scandin., 1921, **55**, 1.
56. Landolt and Bornstein-Roth: Physikalisch Chemische Tabellen, Berlin, 1912, p. 811.
57. Fraenckel, P.: Ztschr. f. klin. Med., 1904, **52**, 470.
58. Gram, H. C.: Jour. Biol. Chem., 1924, **59**, 33.
59. Gram, H. C., and Cullen, G. E.: Jour. Biol. Chem., 1923, **57**, 477.
60. Schmidt, C.: Quoted in Vierordt Anatomische, physiologische und physikalisch chemische Tabellen zum Gebrauche für Mediziner (1906).
61. Naegeli, O.: Blutkrankheiten und Blutdiagnostik, Berlin und Leipzig, 1919.
62. Gram, H. C.: Unpublished figures.
63. Keith, Rowntree and Geraghty: Arch. Int. Med., 1915, **16**, 547
64. Salvesen, H. A.: Jour. Biol. Chem., 1919, **40**, 109.
65. Smith, H. P., Arnold, H. R., and Whipple, G. H.: Am. Jour. Physiol., 1921, **56**.

LOW BACK PAIN AS SEEN IN AN ORTHOPEDIC CLINIC.

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Pain in the low back is a very common complaint among the adult patients who come to a general hospital for treatment. A large percentage of these patients eventually reach the orthopedic department, some of them immediately from the admitting desk, and others by transfer, after having been subjected to a variable amount of study and treatment in other departments.

Anatomically these cases can be divided into lesions of the lumbar and lumbosacral regions and lesions of the sacroiliac joints. Clinically the low back cases fall into three fairly well-defined groups:

1. Cases having definite injury or disease other than chronic arthritis.
2. Chronic arthritis involving the spine and pelvic joints.
3. Strains of the lumbosacral and sacroiliac joints.

The first group comprises tuberculosis of the spine or the sacroiliac joints, neoplasms, fractures (including Kummel's disease), dislocations, Charcot of the spine, acute arthritis of the spine, very rare pyogenic, typhoid, or syphilitic infection of the spine, myositis, contusions, atypical sprains and occasionally a cord or caudal tumor. The entire group makes up only from 5 to 10 per cent of the low back cases. A consideration of each of these conditions is not within the scope of this paper. It will be noted, however, that an early tuberculosis or neoplasm in this region may give signs and symptoms typical of a low back strain, and is usually diagnosed and treated as such until the destruction of bone or abscess makes the true condition evident. And rightly so, because it is better to treat one of these patients for a few weeks or months as a simple strain than to err on the other side and treat fifty strains as a more serious condition.

About 30 to 35 per cent of the low back cases have chronic arthritis, which is usually demonstrable in the roentgenogram. Chronic arthritis of the spine may be divided into:

1. Ankylosing.
2. Atrophic.
3. Hypertrophic.

The ankylosing arthritides of the spine are the spondylose rhizomeliques of Marie and Strumpell, characterized by very little or no pain and involvement of the great joints of the extremities, and the type of von Bechterew, characterized by root pains. The three types merge one into the other. All affect relatively young men, pursue a very chronic course and result in the poker back. The etiology is unknown and the treatment is unsatisfactory. Every effort should be made to prevent flexion deformity. Fortunately these cases are rare.

Atrophic arthritis (rheumatoid arthritis, proliferative arthritis, arthritis deformans) is characterized by fusiform swelling of the joints of the extremities, muscular atrophy, ankylosis with deformities, and bone atrophy. When the spine is involved the roentgenogram shows atrophy of the bone with partial collapse and flaring of the margins of the vertebral bodies. While atrophic arthritis is not uncommon, it is not a frequent cause of low back pain, because the disease is not prone to affect the spine. The etiology is unknown. Cases having low back pain should be given a corset or brace in connection with the treatment of the arthritis.

Hypertrophic arthritis (degenerative or osteoarthritis) is characterized by Heberden's nodes, thickening of the synovia of the involved joints, and the formation of bony spurs or lipping at the

osteocartilaginous margins. It is very prone to attack the spine, and is the great cause of arthritic conditions in the low back. The etiology is unknown. It occurs chiefly in the heavy type of the individual after middle life and tends to progress slowly. There is gradual stiffening, but not ankylosis, of the spine and other joints involved.

The pains in the low back suffered by the hypertrophic cases are, I believe, usually due to strains and not to the arthritis *per se*. The arthritis causes limitation of motion of the spine and renders it more susceptible to strain, but some of the most markedly hypertrophic spines that I have seen were encountered in the routine examination of patients, who stated that they had never been troubled with pain in the low back. Also I have seen a number of patients suffering from acute traumatic strain of the low back in whom the roentgenogram showed advanced hypertrophic changes in the spine, which must have taken a number of years to develop. Many of these patients stated that they had never had pain in the low back until the recent trauma. The indications in these cases are to diagnose the type of strain and then relieve the symptoms by appropriate treatment, as will be mentioned below in considering the back strains. Their body mechanics should be corrected and the back protected from strain, as it is more vulnerable than a normal spine, and recurrences are frequent. An attempt should be made to arrest the arthritis.

The strains of the low back comprise the great majority of the cases coming to the orthopedic clinic complaining of pain in this region. If we include the arthritics whose symptoms are due to strain about 80 to 85 per cent of the low back cases can be classed as strains.

Anatomically they can be divided into lumbosacral (80 to 85 per cent) and sacroiliac (15 to 20 per cent) strains. Clinically the lumbosacral strains can be subdivided into those of sudden onset with known cause, those of gradual onset without known cause and postural strains. The division of each subgroup into acute, recurrent and chronic is an arbitrary measure, because any of them may recur or become chronic. Any case in which the symptoms have persisted for more than four weeks may be considered chronic. Those cases in which a second attack has occurred from a slight cause may be classed as recurrent.

The lumbosacral strains of sudden onset are the most common of the low back strains (35 to 40 per cent of the group). They occur most often in men who are engaged in laborious occupations, though they may occur in women or men of sedentary habits. The patient can usually assign the onset of the pain to a definite cause which may be a severe trauma, such as a fall, wrench of the back or strain incurred in lifting a heavy weight, or it may be only a very minor cause, such as stooping over to pick up a pin from the

floor or getting into a bath-tub. The severity of the symptoms may be out of all proportion to the degree of the trauma. One of the most obstinate cases that I have ever encountered occurred in a strong, able-bodied man, aged thirty-five years, who, one morning, according to his custom, sat on the edge of the bed and leaned over to lace his shoes. All went well until he attempted to straighten up, then he had a severe sharp pain in his low back which caused him to fall to the floor in agony. He remained bedridden for two weeks and then began to hobble about. When I saw him two months later he was considerably disabled and walking with a cane.

As in the case cited above, the initial pain may be very severe and the patient totally disabled for the time being. But this is unusual. The usual history is that the patient had a "stitch" in his back while performing some unusual act and that the pain was not very severe and of short duration. He was conscious of his back from that time on, but paid little attention to it and continued with his work. That evening, or the next day, the pain reappeared and gradually increased in degree. The ultimate condition may be a very mild case in which the patient has a slight unilateral pain in the low back, which is produced by certain movements or positions, or he may be completely disabled by severe pain in the low back and leg.

The character and distribution of the pain are quite characteristic, though its degree and extent are variable. In general, the pain is sharp and lancinating, is aggravated by movement and with rest it may subside entirely or only a dull ache persist. These patients are usually able to assume a position in bed in which they are fairly comfortable, and once having obtained such a position are loath to move. As a rule, they are most comfortable when lying on the unaffected side, with the body, hips and knees moderately flexed, and a pillow between the knees. They have difficulty in turning over in bed at night, but, on the whole, have less pain at night than during the daytime.

In distribution the pain in the beginning is unilateral and most acute at a point just mesial to, and slightly below or above, the posterior-superior spine of the ilium. In the mild cases it remains in this region. In the more severe cases there is apt to be pain on the opposite side and in the lumbar muscles, but it is always most severe on the affected side in the region over the lumbosacral joint and ligaments. In the severe cases it is very common to have the pain appear some days later in the lower extremity on the affected side. This pain is always along the course of nerves whose fibers run in the lumbosacral cord. This gives a distribution in the buttocks along the superior gluteal, in the thigh along the sciatic and in the leg along the external popliteal to the back of the leg and external malleolus. Any or all of the above regions may be affected. These referred pains may be burning in character and in some cases

neurological examination may reveal areas of anesthesia or hyperesthesia. Occasionally the pain in the back entirely disappears, and only the sciatica persists. Many of these patients have had one or more similar attacks of varying severity.

On physical examination these patients are usually strong, healthy men. The objective findings vary directly with the severity of the symptoms. In a severe case the patient is unable to assume the erect posture, but stands with the body bent forward and listed away from the affected side—the so-called sciatic scoliosis. There is marked spasm of the muscles of the low back, the normal lumbar curve is obliterated and only very slight movements are permitted because of the severe pain. In the erect posture there is practically no movement in the low back. There is acute tenderness in the lumbosacral region of the affected side, and pressure here may cause pain in the distribution of the lumbosacral cord. There may be tenderness in the opposite lumbosacral region, in both erector spinæ, and in the buttock, posterior thigh, leg or external malleous of the affected side. Deep abdominal palpation on the affected side may cause pain in the back.

Straight leg raising, full flexion of the hip, internal or external rotation of the flexed hips, hyperextension and Ely's maneuver cause acute pain, and are more limited on the affected side.

The above is a typical picture of a severe case. A mild case will show slight tenderness in the lumbosacral region of the affected side, slight limitation of motion in the low back, slight pain on bending forward, bending toward the affected side and upon straight leg raising. All gradations exist between the mild and very severe types mentioned above. It is to be noted that the physical signs may vary greatly from day to day, and twenty-four hours' rest in bed may produce a very marked change in the picture.

The postural strains of the lumbosacral region are more common in women. The pain is nearly always of gradual onset and without known cause, though in a few cases it follows an illness, a period of heavy work or a marked gain in weight. The condition is chronic, and most of the patients when seen by an orthopedist have been having trouble for some months or even years, not constantly, but from time to time, and especially after unusual physical or mental strain. A considerable number of the women with postural strains also have uterine displacements.

In a postural strain of the lumbosacral region the pain is usually worse at night. Many of these patients have very little pain during the day unless they do an unusual amount of work and get tired; but at night they are awakened by a dull aching pain in the low back, which is only relieved by sitting up in bed, getting up from bed, or a lumbar pillow. Or they may have the pain on getting up in the morning and it wears off in a short time. They start the day all tired out. The location of the pain is character-

istic. It is not referred down the thighs or legs, but is bilateral in the low back and most acute in the lumbosacral region. It may be more marked on one side. The pain is not sharp or burning, but is described as a dull ache, or it may be only a tired feeling.

On physical examination these patients may be of the heavy type with a sharp lumbar lordosis, the normal type with a moderate lumbar lordosis, or the slender type with a long lumbar curve. They may be weak and undernourished, or strong and muscular, or obese. In many of them the posture is very poor, in that they habitually stand with the head forward, shoulders drooped, chest flat, abdomen relaxed, lumbar spine hyperextended, body slumped and the body weight resting upon the heels with the feet pronated. All of them have the fault that they habitually stand with the lumbosacral region at or near the limit of hyperextension for the individual.

As in the lumbosacral strains of sudden onset, the objective findings vary directly with the severity of the symptoms. In the average case there is slight bilateral tenderness to deep pressure in the lumbosacral region, and pain here on hyperextension of the spine or of the hips and slight pain on bending forward. The movements of the spine are not limited. In a severe case there is also some spasm and limitation of motion in the low back and pain on straight leg raising and on lateral bending. In a mild case there may be no pain or tenderness at the time of examination, and all motions of the spine and hips are free and of normal range for the type of individual. Here the diagnosis is made by the history and physical findings which are negative, with the exception of the poor posture.

The above are the two clear-cut groups, and together comprise about 75 per cent of the cases of strain in the lumbosacral region. There is an intermediate group comprising about 25 per cent of these cases, which I term lumbosacral strain of gradual onset. The histories of these cases resemble those of the postural strains in that the pain is of gradual onset and without known cause, and in many of them it is worse at night in bed. Also in character the pain is usually described as a dull ache. On the other hand, the condition is more frequent in men, and the distribution of the pain is that characteristic of the lumbosacral strains of sudden onset, that is, the pain is unilateral in the low back and referred along the course of the fibers of the lumbosacral cord to the superior gluteal, sciatic and external popliteal nerves. As a class, the symptoms are much less than in the lumbosacral strains of sudden onset, though they may extend over a course of years, and at times be fairly acute and necessitate changes in occupation, though rarely ever cause complete disability.

On physical examination, if seen in an acute state, they have a flat back, with spasm in the lumbar muscles, and present the

typical picture of a lumbosacral strain of sudden onset and of moderate severity. In a mild case the poor posture is a prominent feature, but the limitation of motions and the pains elicitated are those characteristic of lumbosacral strain of sudden onset rather than of postural strain.

The sacroiliac strains are, I believe, much less common than is generally supposed. In my experience about 1 in 5 of the low back strains has been classed as a sacroiliac strain. The onset may be acute, with or without trauma, or gradual. The pain is usually severe at night, especially upon turning over in bed, and may be a sharp pain or a dull ache. In others the pain is relieved by recumbency, but is acute on sitting up or walking. It may resemble that of the traumatic lumbosacral strain in distribution, but many of these patients also have pain in the inner side of the upper thigh and occasionally in the pubic region. The point of tenderness is characteristic in that it is located just below and lateral to the posterior-inferior spine, where the lower end of the sacroiliac joint can be palpated through the great sciatic ligament. It is to be remarked that the rest of this joint is protected posteriorly by the overhanging posterior border of the ilium, and tenderness in the neighborhood of the posterior-superior spine is not a sign of trouble in the sacroiliac joint. The same is true of tenderness upon deep abdominal palpation in the region lateral to the sacral promontory. Here the lesion may be either sacroiliac or lumbosacral.

Other than the location of the tenderness below the posterior-inferior spine, the characteristic sign in sacroiliac strain or disease is the ability of the examiner to elicit pain by putting strain upon the sacro-iliac joints without causing movement or strain in the lumbosacral region. This can be done by strongly compressing the anterior-superior spines of the ilia. Lateral compression of the spines strains the posteroinferior portion of the joints, and pressing the spines downward and outward, with the patient supine on a firm table, puts tension upon the anterosuperior portions of the sacroiliacs. If either of these maneuvers, when properly carried out, causes the pain of which the patient complains there is no question but that there is some difficulty in the sacroiliac joints. On rectal examination the lower portion of the joint can be palpated. Acute tenderness here is strong confirmatory evidence of strain or disease in the sacroiliacs. In all other respects the sacroiliac strain may give the clinical picture of a lumbosacral strain.

Roentgenograms are useful to determine the nature and extent of arthritis or other disease of the bone which may be present and to detect congenital anomalies in the lumbosacral region. Congenital anomalies are about five times as frequent in these low back cases as they are in an equal number of patients who do not have low back pain. When present they render the prognosis more grave, as such cases often respond poorly to treatment.

The pathology of these low back strains is unknown. I do not think that they are lesions of the muscles, but am inclined to the belief that the ones of sudden onset are true sprains, with tears of the ligaments or joint capsules. The referred pains are perhaps due to irritation of the fourth and fifth lumbar nerve roots by an exudate or by a synovitis of the adjacent joints. In the postural strains it is possible that the pain is due to irritation of the posterior sacrum caused by pressure of the articular processes of the last lumbar vertebra, which in hyperextension of the spine glide down over their facets to impinge upon the sacrum.

In treating these cases it is important to decide whether the lesion is lumbosacral or sacroiliac or both, and then direct the treatment to the involved region. An acute strain demands fixation and rest in bed, usually with sedatives. A firm strapping with adhesive plaster is often sufficient fixation if the patient will remain in bed for a few days. For a sacroiliac the strapping need not extend above the iliac crests, but for the lumbosacral it should extend up to the dorsolumbar region. Hot fomentations or other forms of local heat are often helpful. In bed a lumbar pillow and a pillow under the knees may be beneficial. For ambulatory treatment a narrow sacroiliac belt is used for the sacroiliac cases and a wide lumbosacral belt or low back brace is used for the lumbosacrals. In women the belt or brace can be incorporated in the corset or worn beneath it. Plaster jackets are seldom used, as it is extremely difficult to apply an ambulatory jacket which fixes either of these regions. The average case does well under the above treatment, but occasionally one meets a very resistant case in which prolonged rest in bed is necessary to effect a cure. Some of these difficult cases are helped by manipulation under full anesthesia; others are not. In some chronic sacroiliacs it may be necessary to arthrodese the joint. This is best done by the Smith-Peterson method.

In the postural strains the acute symptoms demand support to the low back just as do the traumatic type of the lumbosacral strains. A permanent cure, however, is only obtained by correcting the poor posture. This is accomplished by a course of exercises directed to the correction of the body mechanics. The object of the orthopedist in treating these low back strains is first to relieve the symptoms, then to correct the mechanics of the low back and strengthen it by exercises until the patient is able to live a normal life, without any permanent supporting apparatus.

Summary. Low back pain and sciatica are frequent complaints among orthopedic patients. In the great majority of these cases the symptoms are due to strain in the lumbosacral or sacroiliac regions.

The lumbosacral strains are about four times as frequent as are those of the sacroiliac joints. Occasionally both regions are

involved. These low back strains may be due to trauma or to postural defects, and they may be acute or chronic. In patients beyond middle life hypertrophic arthritis of the spine is a frequent complication. The mode of onset, character and distribution of the pain, the location of the tenderness, the limitations of motion and the pain elicited by movement of the spines and hips are characteristic for each type of strain. There are, however, wide variations in the severity of the symptoms in strains which are essentially of the same type.

The diagnosis of the type of strain is made from the history and physical findings. A roentgenogram is of value in ruling out injury or disease of the bone, in determining the extent of arthritic changes, if present, and in detecting congenital anomalies of the spine. It does not differentiate between lumbosacral and sacroiliac strains. Sacroiliac luxation with slight displacement, demonstrable by the roentgen-ray, apparently does not occur. The characteristic symptoms and physical findings of each type of sprain are given above.

In the treatment it is important to make a definite diagnosis if possible and direct the therapy accordingly. The objects of treatment are relief from pain, resumption of normal activity and prevention of recurrence. Sedatives, rest in bed, support to the strained region, corrective exercises and physiotherapy are used in handling these cases. In arthritic cases the arthritis also should receive attention.

The prognosis is, as a rule, good. Chronic and recurring cases usually require a longer time for cure. Sacralization of the fifth lumbar vertebra makes the prognosis more grave, as these cases may be prolonged and difficult to relieve. Arthritis of the spine renders recurrence more likely.

THE THERAPEUTIC VALUE OF BLOOD TRANSFUSION.

With Report of Sixty-eight Cases of Sepsis.

By Rufus E. Stetson, M.D.,
NEW YORK.

Ten years have passed since the development of blood transfusion from an uncertain, prolonged and delicate surgical operation, not without danger, to a quick, safe and comparatively simple procedure. During this time several methods of handling blood have been devised, and much has been said and written *pro* and *con* as regards their respective advantages.

Whole blood *versus* citrated blood has been the basis for more discussion than any other problem in this field of work, and for several years following its introduction the citrate method increased in popularity because of the greater ease of its accomplishment by untrained operators. Today the great majority of men prefer whole-blood methods because it is the safer method. It has been demonstrated beyond the shadow of a doubt that the use of citrated blood is accompanied by severe reactions in more than 50 per cent of the transfusions performed, and in some cases death has ensued as a result.

The cause or causes of posttransfusion reactions have been very thoroughly investigated. These vary from the lesser febrile reactions to the severe chill and high temperature with great prostration.

Novy and Dekrief[1] believe that the matrix of the poison anaphylactic toxin is in the plasma and serum of the blood, and they say that the disturbance which brings about the transformation of the matrix into poison is readily affected by the addition of almost any alien substance, even physiological salt solution. They also showed that toxic substances develop in blood on standing for a period of three minutes.

Drinker and Brittingham,[2] on the other hand, found that the blood platelets apparently have more to do with reactions than the serum, but that these early coagulation changes take place when the blood is kept out of its natural element for from three to five minutes, even in the presence of an anticoagulant, such as sodium citrate. They also showed that the mere addition of sodium citrate to blood causes slight abnormality of the red blood cells, increasing their fragility and tendency to hemolysis.

Unger[3] confirmed and elaborated their findings as regards the effect of sodium citrate on red blood cells, and in his conclusion states that "Sodium citrate, even in the low percentage employed in a citrate transfusion, effects the red blood cells, rendering them more fragile, and the value of such blood to a patient suffering from a hemolytic disease, such as pernicious anemia, is lessened to that extent." Whether these toxic properties belong to the plasma, the red cells or the platelets, it is the concensus of opinion that the addition of any alien substance, even physiological salt solution to the blood, or the keeping of the blood out of its natural element for from three to five minutes, may activate these toxic properties.

Bernheim,[4] of Baltimore, who had charge of the transfusion work in the A. E. F., where nothing but citrated blood was used, gave a fair and unbiased discussion of this subject. He says, "We must not be blind to the fact that the sodium-citrate-blood transfusion possesses certain obscure, but none the less inherent, features that are not only embarrassing to the physician, but most uncomfortable and even dangerous to the patient. Chills and fever and profound shock have never helped anyone, and to ignore the danger

neurological examination may reveal areas of anesthesia or hyperesthesia. Occasionally the pain in the back entirely disappears, and only the sciatica persists. Many of these patients have had one or more similar attacks of varying severity.

On physical examination these patients are usually strong, healthy men. The objective findings vary directly with the severity of the symptoms. In a severe case the patient is unable to assume the erect posture, but stands with the body bent forward and listed away from the affected side—the so-called sciatic scoliosis. There is marked spasm of the muscles of the low back, the normal lumbar curve is obliterated and only very slight movements are permitted because of the severe pain. In the erect posture there is practically no movement in the low back. There is acute tenderness in the lumbosacral region of the affected side, and pressure here may cause pain in the distribution of the lumbosacral cord. There may be tenderness in the opposite lumbosacral region, in both erector spinæ, and in the buttock, posterior thigh, leg or external malleous of the affected side. Deep abdominal palpation on the affected side may cause pain in the back.

Straight leg raising, full flexion of the hip, internal or external rotation of the flexed hips, hyperextension and Ely's maneuver cause acute pain, and are more limited on the affected side.

The above is a typical picture of a severe case. A mild case will show slight tenderness in the lumbosacral region of the affected side, slight limitation of motion in the low back, slight pain on bending forward, bending toward the affected side and upon straight leg raising. All gradations exist between the mild and very severe types mentioned above. It is to be noted that the physical signs may vary greatly from day to day, and twenty-four hours' rest in bed may produce a very marked change in the picture.

The postural strains of the lumbosacral region are more common in women. The pain is nearly always of gradual onset and without known cause, though in a few cases it follows an illness, a period of heavy work or a marked gain in weight. The condition is chronic, and most of the patients when seen by an orthopedist have been having trouble for some months or even years, not constantly, but from time to time, and especially after unusual physical or mental strain. A considerable number of the women with postural strains also have uterine displacements.

In a postural strain of the lumbosacral region the pain is usually worse at night. Many of these patients have very little pain during the day unless they do an unusual amount of work and get tired; but at night they are awakened by a dull aching pain in the low back, which is only relieved by sitting up in bed, getting up from bed, or a lumbar pillow. Or they may have the pain on getting up in the morning and it wears off in a short time. They start the day all tired out. The location of the pain is character-

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The above are the two clear-cut groups, and together comprise about 75 per cent of the cases of strain in the lumbosacral region. There is an intermediate group comprising about 25 per cent of these cases, which I term lumbosacral strain of gradual onset. The histories of these cases resemble those of the postural strains in that the pain is of gradual onset and without known cause, and in many of them it is worse at night in bed. Also in character the pain is usually described as a dull ache. On the other hand, the condition is more frequent in men, and the distribution of the pain is that characteristic of the lumbosacral strains of sudden onset, that is, the pain is unilateral in the low back and referred along the course of the fibers of the lumbosacral cord to the superior gluteal, sciatic and external popliteal nerves. As a class, the symptoms are much less than in the lumbosacral strains of sudden onset, though they may extend over a course of years, and at times be fairly acute and necessitate changes in occupation, though rarely ever cause complete disability.

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Roentgenograms are useful to determine the nature and extent of arthritis or other disease of the bone which may be present and to detect congenital anomalies in the lumbosacral region. Congenital anomalies are about five times as frequent in these low back cases as they are in an equal number of patients who do not have low back pain. When present they render the prognosis more grave, as such cases often respond poorly to treatment.

The pathology of these low back strains is unknown. I do not think that they are lesions of the muscles, but am inclined to the belief that the ones of sudden onset are true sprains, with tears of the ligaments or joint capsules. The referred pains are perhaps due to irritation of the fourth and fifth lumbar nerve roots by an exudate or by a synovitis of the adjacent joints. In the postural strains it is possible that the pain is due to irritation of the posterior sacrum caused by pressure of the articular processes of the last lumbar vertebra, which in hyperextension of the spine glide down over their facets to impinge upon the sacrum.

In treating these cases it is important to decide whether the lesion is lumbosacral or sacroiliac or both, and then direct the treatment to the involved region. An acute strain demands fixation and rest in bed, usually with sedatives. A firm strapping with adhesive plaster is often sufficient fixation if the patient will remain in bed for a few days. For a sacroiliac the strapping need not extend above the iliac crests, but for the lumbosacral it should extend up to the dorsolumbar region. Hot fomentations or other forms of local heat are often helpful. In bed a lumbar pillow and a pillow under the knees may be beneficial. For ambulatory treatment a narrow sacroiliac belt is used for the sacroiliac cases and a wide lumbosacral belt or low back brace is used for the lumbosacrals. In women the belt or brace can be incorporated in the corset or worn beneath it. Plaster jackets are seldom used, as it is extremely difficult to apply an ambulatory jacket which fixes either of these regions. The average case does well under the above treatment, but occasionally one meets a very resistant case in which prolonged rest in bed is necessary to effect a cure. Some of these difficult cases are helped by manipulation under full anesthesia; others are not. In some chronic sacroiliacs it may be necessary to arthrodese the joint. This is best done by the Smith-Peterson method.

In the postural strains the acute symptoms demand support to the low back just as do the traumatic type of the lumbosacral strains. A permanent cure, however, is only obtained by correcting the poor posture. This is accomplished by a course of exercises directed to the correction of the body mechanics. The object of the orthopedist in treating these low back strains is first to relieve the symptoms, then to correct the mechanics of the low back and strengthen it by exercises until the patient is able to live a normal life, without any permanent supporting apparatus.

Summary. Low back pain and sciatica are frequent complaints among orthopedic patients. In the great majority of these cases the symptoms are due to strain in the lumbosacral or sacroiliac regions.

The lumbosacral strains are about four times as frequent as are those of the sacroiliac joints. Occasionally both regions are

involved. These low back strains may be due to trauma or to postural defects, and they may be acute or chronic. In patients beyond middle life hypertrophic arthritis of the spine is a frequent complication. The mode of onset, character and distribution of the pain, the location of the tenderness, the limitations of motion and the pain elicited by movement of the spines and hips are characteristic for each type of strain. There are, however, wide variations in the severity of the symptoms in strains which are essentially of the same type.

The diagnosis of the type of strain is made from the history and physical findings. A roentgenogram is of value in ruling out injury or disease of the bone, in determining the extent of arthritic changes, if present, and in detecting congenital anomalies of the spine. It does not differentiate between lumbosacral and sacroiliac strains. Sacroiliac luxation with slight displacement, demonstrable by the roentgen-ray, apparently does not occur. The characteristic symptoms and physical findings of each type of sprain are given above.

In the treatment it is important to make a definite diagnosis if possible and direct the therapy accordingly. The objects of treatment are relief from pain, resumption of normal activity and prevention of recurrence. Sedatives, rest in bed, support to the strained region, corrective exercises and physiotherapy are used in handling these cases. In arthritic cases the arthritis also should receive attention.

The prognosis is, as a rule, good. Chronic and recurring cases usually require a longer time for cure. Sacralization of the fifth lumbar vertebra makes the prognosis more grave, as these cases may be prolonged and difficult to relieve. Arthritis of the spine renders recurrence more likely.

THE THERAPEUTIC VALUE OF BLOOD TRANSFUSION.

With Report of Sixty-eight Cases of Sepsis.

By Rufus E. Stetson, M.D.,
NEW YORK.

Ten years have passed since the development of blood transfusion from an uncertain, prolonged and delicate surgical operation, not without danger, to a quick, safe and comparatively simple procedure. During this time several methods of handling blood have been devised, and much has been said and written *pro* and *con* as regards their respective advantages.

Whole blood *versus* citrated blood has been the basis for more discussion than any other problem in this field of work, and for several years following its introduction the citrate method increased in popularity because of the greater ease of its accomplishment by untrained operators. Today the great majority of men prefer whole-blood methods because it is the safer method. It has been demonstrated beyond the shadow of a doubt that the use of citrated blood is accompanied by severe reactions in more than 50 per cent of the transfusions performed, and in some cases death has ensued as a result.

The cause or causes of posttransfusion reactions have been very thoroughly investigated. These vary from the lesser febrile reactions to the severe chill and high temperature with great prostration.

Novy and Dekrief[1] believe that the matrix of the poison anaphylactic toxin is in the plasma and serum of the blood, and they say that the disturbance which brings about the transformation of the matrix into poison is readily affected by the addition of almost any alien substance, even physiological salt solution. They also showed that toxic substances develop in blood on standing for a period of three minutes.

Drinker and Brittingham,[2] on the other hand, found that the blood platelets apparently have more to do with reactions than the serum, but that these early coagulation changes take place when the blood is kept out of its natural element for from three to five minutes, even in the presence of an anticoagulant, such as sodium citrate. They also showed that the mere addition of sodium citrate to blood causes slight abnormality of the red blood cells, increasing their fragility and tendency to hemolysis.

Unger[3] confirmed and elaborated their findings as regards the effect of sodium citrate on red blood cells, and in his conclusion states that "Sodium citrate, even in the low percentage employed in a citrate transfusion, effects the red blood cells, rendering them more fragile, and the value of such blood to a patient suffering from a hemolytic disease, such as pernicious anemia, is lessened to that extent." Whether these toxic properties belong to the plasma, the red cells or the platelets, it is the concensus of opinion that the addition of any alien substance, even physiological salt solution to the blood, or the keeping of the blood out of its natural element for from three to five minutes, may activate these toxic properties.

Bernheim,[4] of Baltimore, who had charge of the transfusion work in the A. E. F., where nothing but citrated blood was used, gave a fair and unbiased discussion of this subject. He says, "We must not be blind to the fact that the sodium-citrate-blood transfusion possesses certain obscure, but none the less inherent, features that are not only embarrassing to the physician, but most uncomfortable and even dangerous to the patient. Chills and fever and profound shock have never helped anyone, and to ignore the danger

of these sequelæ, merely to note their occurrence without vouchsafing a careful consideration of their eventualities, is little more than admitting a mind closed to certain embarrassing features connected with the procedure." And in conclusion he remarks: "I would not have you think for one moment that this is an attempt to belittle the value of the citrate transfusion—no one realizes better than I how much that has meant to the medical professional and to humanity at large—but it is necessary to recognize the fact that there are definite limitations to this method of giving blood, and that failure to observe these limitations has caused unnecessary loss of life. There should be in every community at least one man who is competent to carry out the whole-blood method, and physicians should learn to differentiate their cases so that they may take advantage of this man's skill and give their charges that chance for life for which they come to him."

Dr. Bernheim is a man of wide experience not only in general surgery, but one who has performed many blood transfusions himself, and who, in June, 1917, read a paper before the American Medical Association advocating the general adoption of the citrate method. It is, therefore, particularly gratifying when such a man comes out with such conclusive support of the opinion long held by Lindeman, Unger and other workers in this field, including the author.

My preference for the syringe cannula method is based on the fact that it is the most flexible and quickest and injures the blood as little as any other method, and with a little training is the easiest to accomplish. Three things are necessary to this operation as to any other, that is, perfect instruments, accurate knowledge of the technic in all its details and practice. The first two essentials are not difficult of attainment, and a very moderate amount of practice will enable one to accomplish the operation successfully. It is less dependent on mechanical factors than any other method because there is less apparatus. The blood is out of its natural element only about ten to fifteen seconds, or just the length of time it takes to transfer a single syringeful, no matter whether you give 20 cc or 2 liters, as I have done on more than one occasion. One can give as much or as little blood as the condition of the patient may justify during the operation without wasting any blood, or the procedure may be halted at any time to observe the effect on patient or donor and then resumed without any break in technic. Two assistants, one trained in the technic of withdrawing blood from the donor and one untrained, for the washing of the syringes are desirable but not essential, as I have accomplished the entire procedure unassisted. The special cannulæ, three to five 20-cc record syringes and four basins of sterile normal salt solution is all the apparatus necessary.

Indications for Transfusion. Transfusion is coming to be used more and more as a therapeutic measure, but much progress

remains to be made in the profession at large in getting away from the idea that it is a measure to be used only as a last resort. It is useful in the following conditions.

Hemorrhage.

Hemorrhage, acute and chronic.
Hemorrhage of the newborn.
Purpura.
Hemophilia.

Anemias.

Secondary anemia:
- Pregnancy or puerperium.
- Chronic surgical cases:
  - Empyema.
  - Burns.
  - Traumatic.
- Malnutrition.

Pernicious anemia.
von Jakschs' anemia.

Sepsis.

Acute or chronic:
- Osteomyelitis.
- Multiple arthritis.
- Multiple abscesses.
- Postoperative:
  - Mastoid sinus or jugular thrombosis.
  - Tonsillectomy.
- Puerperal.

Toxemia.

Pneumonia.
Typhoid.
Scarlet fever.
Nephritis.
Acute infections.

Jaundice.

To reduce clotting-time of blood if operative procedure is indicated.
To overcome toxemia.

Miscellaneous.

Gas-poisoning.
Drug addiction.
Shock in operative procedures.

We have employed it successfully in typhoid fever to combat the severe toxemias as well as hemorrhage, and I have had 2 cases of encephalitis complicating scarlet fever, both of which recovered—1 after six transfusions and the other after two. Both had severe convulsions, controlled only by chloroform, and were extremely ill; both showed marked and steady improvement as soon as the transfusions were started.

I no longer advise transfusions in acute lymphatic leukemia, as it is a very temporary help, and life is rarely prolonged more than a few weeks.

Transfusion for Hemorrhage. The results in hemorrhage are naturally the most uniformly successful and often the most dramatic. Obstetrical and gynecological conditions furnish the largest proportion of acute hemorrhage cases. It has long been my contention that every expectant mother should have her blood group determined in order to save valuable and perhaps vital time in case of need. I recall 4 fairly recent cases which will serve as good examples of this group. Three of them occurred in the practice of the same man, a surgeon of Jersey City.

The first case was a woman, of middle age, who had carried a slow-growing fibroid for several years without any symptoms except the gradually increasing size of the abdomen. She finally came to the physician last summer for excessive bleeding. The tumor by that time had reached an enormous size, filling the whole lower abdominal cavity, and it was decided to try to reduce it in size by radium before operating. Treatment was accordingly started, and marked reduction in the size of the tumor was soon noted, but the bleeding got worse instead of better, and I was called to transfuse her on July 29, 1922. No blood count was done, but she was extremely anemic and very weak. She was given 1000 cc of blood, and, while there was immediate improvement, the bleeding failed to stop, and she was given 1200 cc of blood on September 9. A few more days' observation, with no check in the bleeding, made it evident that operative interference was imperative; consequently, I went over on September 15 with two donors and, after giving 650 cc of blood, a hysterectomy was performed and, though greatly reduced in size, the fibroid then removed was as large as a good-sized pumpkin. Immediately following the operation the patient was given 500 cc more blood from the second donor, a total of 1150 cc, and she made a quick, uneventful and complete recovery.

The second case was one of incomplete abortion, with severe hemorrhage. A consultant was called, and the patient was hurried to a hospital; meanwhile a specimen of blood for grouping was sent to me. No time was wasted, but when I arrived the woman was semicomatose and in very poor condition. She was given 1000 cc of blood, and when we finished she was laughing and talking, and went through a curettage the next morning without any trouble.

The third case was in a woman, aged forty-one years, with no previous history of bleeding. She had had two or three miscarriages but no children. At her last period two or three weeks previous she had bled only one day instead of several as usual. Her bleeding began suddenly and was quite profuse. A physician was called in consultation and, while a definite diagnosis could not be made, he suspected a ruptured ectopic and felt that an exploratory laparotomy was indicated. Her condition by that time made her an extremely poor operative risk, so I was asked to come prepared to transfuse before and after operation as I had done in the

first case. She was given 800 cc and as soon as the needle was withdrawn from her vein the anesthetic was started. A hysterectomy was performed, and it was discovered that all her trouble was from a small submucous fibroid. She stood the operation very well, and after receiving 500 cc more of blood was sent back to the ward in excellent condition.

The lives of all 3 of these women were undoubtedly saved by transfusion, but I mention them particularly because of the fact that not only was severe hemorrhage successfully combated, but also because extremely poor operative risks were thereby transformed into very good risks. The surgeon's nerves were saved considerable wear and tear and his reputation enhanced.

The fourth case is an argument in favor of blood-typing of all pregnant women, and an example of the danger of transfusing without doing tests. The case was that of a young healthy woman of the poorer class. It was during the sixth month of her first pregnancy, during which she probably had had very little medical attention. At any rate she was brought into the Manhattan Maternity one evening as an emergency. She was found to be a case of placenta previa, and bleeding profusely. The uterus was emptied as expeditiously as possible, but not, of course, without considerable additional loss of blood, which left her in a very precarious condition. I was called and found her almost pulseless, semicomatose and apparently dying. The patient's mother was the only relative present, and it is interesting to note that the daughter bore a striking physical resemblance to her. It seemed like a case where we were justified in transfusing without a moment's delay; consequently, preparations were quickly made, and the transfusion started with the mother as donor. Only two syringefuls of blood, 40 cc, had been introduced when the patient evinced signs of distress, drawing up her knees and groaning, followed by vomiting and extreme cyanosis, which with her pallor gave her a positively green appearance. I immediately stopped the transfusion and gave her 750 cc of physiological salt solution. She rallied temporarily but died in about two hours, before tests could be completed and the proper donor secured. Before starting the transfusion I had taken specimens from both mother and daughter, and subsequent tests proved them to belong to totally different blood groups.

Transfusion in Anemias. There is a peculiar type of anemia which sometimes occurs during pregnancy or the puerperium, perhaps due to the strain put upon the hemopoietic system or it may be an endocrine disturbance; however that may be, it cannot be differentiated from pernicious anemia so far as the blood-picture goes, but is permanently corrected by transfusion.

In the past three and a half years I have had the opportunity to treat 92 cases of pernicious anemia. In all 294 transfusions were performed on these 92 patients, from one to twenty-six transfusions being given to the individual case. The total quantity of blood

transfused was 326,420 cc or 326½ liters, from 650 cc to 2300 cc (2 donors) being given at a time—an average of over 1100 cc for each transfusion.

In 8 of the patients the course of the disease was not appreciably affected, death occurring within one to six weeks. One of these patients had two transfusions and 7 had but one. In 2 patients I have no record as to how long their improvement lasted. In 56 patients it was possible to prolong life from three months to two years and to relieve them of their most distressing symptoms, though without definite remissions. One of these patients in a year and ten months required twenty-six transfusions, a total of 30½ liters of blood, but during the major part of that time he was kept fairly comfortable and active enough to settle his important business affairs. Life cannot be measured in dollars and cents, but, as in this case, even a few months' prolongation of life may be of distinct economic value to those intimately concerned. In the remaining 23 cases one or more remissions have occurred. The shortest, three months' duration; the longest in this series, two years, and still continuing. Four are having their second remission, having now gone sixteen, ten, nine and eight months respectively.

It seems evident that no other therapeutic measure has the power and efficacy that transfusion of unmodified blood has in treating pernicious anemia. It is indicated whenever the hemoglobin reaches 35 or 40 per cent and whenever distressing symptoms arise, even when occurring at a much higher level. Amounts of 1000 cc or over of unmodified blood give the best results, for by using large amounts we obtain the maximum improvement both in the blood and in the general condition of the patient and also give them a much longer interval between transfusions.

Transfusion is always indicated in idiopathic purpura hemorrhagica, but my experience has been that it is very likely to go on to a fatal termination in spite of everything that may be done. It is an absolute, though not permanent, specific in hemophilia. In bleeding of the newborn the hemorrhage is not only controlled, but the effect is lasting.

Most of the von Jakschs' anemias do very well after transfusion.

We have 2 patients with Hodgkin's disease still living that did very well. In both instances the febrile crises, occurring every ten days or so, were checked, and a definite remission induced in 1 patient, while the other has at least been kept alive and is being given radium and roentgen-ray therapy.

Transfusion in Sepsis. We see a good deal of chronic empyema and osteomyelitis on the Children's Surgical Service at Bellevue Hospital, and these cases are apt to be in extremely poor condition when referred to me. They have a marked secondary anemia, and their wounds respond very sluggishly to treatment. They may be quite toxic from absorption, and often their appetite and digestion are poor. It is most gratifying to see how well these children do with

an occasional transfusion. Their secondary anemia is overcome, their appetite and digestion immediately improve and in a surprisingly short time their wounds begin a healthy granulation. The danger of intercurrent infections is also lessened and their convalescence greatly shortened.

This is also true of the bad traumatic cases and some of the burn cases that have a long drawn-out convalescence.

Some of the bad malnutrition cases on the infants' service are also saved by transfusion.

The following is a partial report of my work on sepsis. It seems to me that the results in this condition are of the greatest importance because of the seriousness of the condition we have to combat. In the past we had to depend almost wholly on the natural strength and resistance of the patient, and even today, in spite of vaccines, serums and colloids, we would be just about as helpless as ever in the face of acute sepsis were it not for blood transfusion.

Lindeman was the first to prove this, and it was his good work that first convinced me of the efficacy of the measure. I know there has been some debate on this matter and that it has not proved successful in all hands. We received no heaven-sent inspiration on how to use blood therapy, but through experience we have learned how to apply the measure to the best advantage and have succeeded in cutting down the mortality in sepsis by a substantial percentage.

In using blood therapy to combat sepsis we have a two-edged weapon: The power it has to overcome the secondary anemia and build up the general condition of the patient and the direct bactericidal action of the fresh blood on the infecting organism. The latter factor is, of course, the more variable, depending on the virulence and character of the organism, the focus of infection and the phagocytic power of the blood employed, but I have observed steady diminution in the number of colonies and final sterilization of the blood stream in a sufficient number of cases to convince me that normal blood has a very real value as a bactericidal agent.

The use of immunized donors should theoretically be much more effective, but in the cases I have observed the results did not seem to justify this belief, and the elements entering into the production of immunity either actively in the patient or passively in the case of the donor are so complex and so little understood that we cannot argue convincingly from a laboratory point of view. We are forced, as indeed is so often the case, to take the clinical results as our ultimate, deciding factor. It is only fair to say, however, that the difficulties in the way of immunizing donors in time to be of any use in acute sepsis has made it impossible to employ this method in a conclusive number of cases.

I have treated by blood transfusion about 100 cases of undoubted sepsis. The group of 68 cases that are included in this report were not selected but were taken indiscriminately. Many of these cases

were from the wards of Bellevue Hospital, and were much poorer material to work with in the beginning than one usually encounters in private practice.

The cases will be studied first from a bacteriological viewpoint and then according to the clinical diagnosis.

Thirty-nine of the cases showed positive blood cultures (Chart I). Streptococcus hemolyticus occurred in 19 instances, with 10 recoveries and 9 deaths. Of the 9 patients that died pneumonia killed 4 and meningitis developed in 2.

CHART I.

Patients.	Diagnosis.	Blood cultures positive for.	No. of transfusions.	Result.
1	Malignant endocarditis	Streptococcus viridans	6	Died.
2	Malignant endocarditis	Streptococcus viridans	7	Died.
3	Malignant endocarditis	Streptococcus viridans	2	Died.
4	Malignant endocarditis	Streptococcus viridans	1	Died.
5	Malignant endocarditis	Streptococcus viridans	1	Died.
6	Malignant endocarditis	Staphylococcus aureus	1	Died.
7	Malignant endocarditis	Streptococcus viridans	7	Died.
8	Mastoid with sinus and jugular thrombosis	Streptococcus hemolyticus	2	Recovered.
9	Mastoid with sinus and jugular thrombosis	Streptococcus hemolyticus	3	Recovered.
10	Mastoid, sinus thrombosis, pneumonia, empyema, acute nephritis	Streptococcus hemolyticus	5	Recovered.
11	Mastoid, sinus thrombosis, pneumonia, empyema	Streptococcus hemolyticus	3	Recovered.
12	Mastoid, sinus thrombosis	Streptococcus hemolyticus	2	Recovered.
13	Mastoid, sinus thrombosis	Streptococcus hemolyticus	2	Recovered.
14	Mastoid, sinus thrombosis	Streptococcus hemolyticus	3	Recovered.
15	Mastoid, jugular thrombosis	Streptococcus hemolyticus	2	Recovered.
16	Mastoid, jugular thrombosis	Streptococcus hemolyticus	3	Recovered.
17	Mastoid, jugular thrombosis	Streptococcus hemolyticus	1	Died.
18	Mastoid, sinus thrombosis	Streptococcus hemolyticus	2	Died.
19	Mastoid, sinus thrombosis	Streptococcus hemolyticus	6	Died of pneumonia.
20	Mastoid, sinus thrombosis	Streptococcus hemolyticus	4	Died of pneumonia.
21	Scarlet fever, mastoid and sinus thrombosis	Streptococcus hemolyticus	7	Died of pneumonia.
22	Mastoid, sinus thrombosis	Streptococcus hemolyticus	4	Died of meningitis.
23	Postpartum sepsis and osteomyelitis	Streptococcus hemolyticus	2	Recovered.
24	General sepsis with initial focus in cervical glands	Streptococcus hemolyticus	4	Died.
25	General sepsis with initial focus in cervical glands	Streptococcus hemolyticus	9	Died of meningitis.

Patients.	Diagnosis.	Blood cultures positive for.	No. of transfusions.	Result.
26	Postpartum sepsis, pneumonia, gangrene of lung	Streptococcus hemolyticus	4	Died of pneumonia.
27	Post abortion sepsis	Streptococcus viridans	8	Died.
28	Sepsis following tonsillectomy	Streptococcus viridans	2	Recovered.
29	Acute multiple osteomyelitis, multiple abscesses, pyopericarditis	Staphylococcus aureus	16	Died.
30	Acute multiple osteomyelitis	Staphylococcus aureus	11	Recovered.
31	Cellulitis of face	Staphylococcus aureus	1	Died, moribund time of transfusion.
32	Postpartum sepsis	Staphylococcus aureus	1	Died (moribund).
33	Cellulitis of face	Staphylococcus aureus	5	Died.
34	Cellulitis of leg	Staphylococcus aureus	2	Died.
35	Maxillary sinusitis	Staphylococcus aureus	2	Recovered.
36	Post operative appendix	Staphylococcus aureus	1	Died (moribund).
37	Postpartum sepsis	Staphylococcus aureus	2	Died.
38	Frontal sinusitis brain abscess	Staphylococcus aureus	4	Died, meningitis.
39	Acute osteomyelitis	Staphylococcus aureus	2	Recovered.

Streptococcus viridans occurred in 8 cases, 6 of them being malignant endocarditis and fatal in termination. The seventh occurred in a baby, after tonsillectomy, who recovered after two transfusions. The eighth patient had a postpartum sepsis, and died.

Staphylococcus aureus which, contrary to popular belief, is, in my experience the deadliest of the infecting organisms in general sepsis, occurred in 12 patients, 9 of whom died and only 3 recovered. Of the 9 deaths, however, 3 were moribund at the time of the first transfusion, and 1 had an acute endocarditis, so that in at least 4 cases we never had a chance, and a fairer ratio would be 3 recoveries to 5 deaths. The total figures in this group show 14 recoveries to 25 deaths, or 36 per cent of recoveries, with a mortality of 64 per cent.

	Patients.	Recoveries.	Per cent.	Deaths.	No.
Streptococcus hemolyticus	19	10	55.0	Pneumonia	4
				Meningitis	3
				Sepsis	2
Streptococcus viridans	8	1	12.5	Malignant endocarditis	6
				Puerperal sepsis	1
Staphylococcus aureus	12	3	25.0	Moribund	3
				Malignant endocarditis	1
				Pyopericarditis	1
				Cellulitis	2
				Puerperal sepsis	1
				Meningitis	1
Total	39	14	36.0		25

If, however, we substract, as I feel we have a right to do, the 3 moribund patients and the 7 patients with malignant endocarditis

it leaves 14 recoveries to 15 deaths, or practically a mortality of only 51 per cent.

Considered from a diagnostic viewpoint, there were in the streptococcus hemolytic group 14 patients with mastoid and sinus or jugular thrombosis or both, and of these 9 recovered and 5 died. In 2 of the patients that recovered we carried them through a complicating pneumonia and empyema. Of the 5 we lost 2 died of pneumonia and 1 of meningitis. In the remaining 5 cases of Streptococcus hemolyticus 2 started from glands of the neck. In 2 patients with puerperal sepsis the Streptococcus hemolyticus was isolated and 1 recovered, though she had a complicating osteomyelitis. The other died, after we thought she was safe, of gangrene of the lung following a pneumonia. The fifth patient had a bad suppurative arthritis of the knee which we lost. It is interesting to note that of the Streptococcus hemolyticus 73 per cent were in mastoid patients, and that of these more than 64 per cent recovered. The excellent results in this type of case are due no doubt to the fact that the surgeon is able to remove the septic thrombus from vein or sinus, but only in observing the majority of these cases clinically can one appreciate the part blood therapy plays in their recovery.

The Streptococcus viridans was, with 2 exceptions, confined to the malignant endocarditis cases (6 in all), and so far as my experience goes they invariably die. One exception previously mentioned was in the case of the baby following tonsillectomy, which recovered. The other followed abortion. We transfused her eight times but lost her, though it may be permissible to add that the conditions under which we were working were not of the best.

In its malignant form Staphylococcus aureus can kill more quickly and resist treatment more stubbornly than any of the common organisms with which I have come in contact. Undoubtedly there are more superficial localized infections from this organism than any other, but fortunately its tendency is to remain localized and clear up readily under treatment. Of the 12 patients in which this organism was isolated 3 started as a cellulitis—2 of the face and 1 of the leg—following the scratching or picking of an insignificant looking pustule. All 3 died, 1 being moribund at time of transfusion. Three were suffering from a multiple osteomyelitis. One required eleven transfusions but recovered, the second recovered after two transfusions and the third we lost after sixteen transfusions from a pyopericarditis.*

Two patients with puerperal sepsis showed staphylococcus and both died. Two started as sinusitis: One a maxillary, which recovered; the other frontal, which died of meningitis following a successful operation for abscess of the brain. One case developed

* Since this paper was written we have had a similar case of multiple osteomyelitis with positive blood culture for Staphylococcus aureus and complicating pyopericarditis which recovered after nine transfusions.

staphylococcus septicemia following an appendectomy and died, and the last was apparently an acute endocarditis, though no autopsy was performed.

In 29 of these 68 cases either no blood culture was obtained or the cultures were sterile, but no cases have been included that were not unanimously considered sepsis by all who saw them. Exception might be made of 2 cases of gas-bacillus infection following amputation of the leg after traumatic injury in both instances. One patient recovered and the other died of pneumonia after four transfusions and when the stump had regained a healthy granulating appearance and all crepitation had disappeared from the surrounding tissues. At any rate their inclusion does not affect the ratio of our recoveries and deaths (Chart II).

CHART II.—SHOWING CASES IN WHICH THE INFECTING ORGANISM WAS NOT RECOVERED FROM THE BLOOD.

Diagnosis.	No. of cases.	Recoveries.	Deaths.	
Mastoid with sinus or jugular thrombosis	7	3	4	2 died of pneumonia.
Postabortion or puerperal sepsis	14	9	5	2 moribund at time of transfusion; 2 died of pneumonia
Empyema	1	1	0	
Influenza	1	1	0	
Osteomyelitis	2	2	0	
Suppurative arthritis	1	0	1	
Endocarditis	1	0	1	
Gas bacillus infection	2	1	1	Died of pneumonia.
	29	17	12	

There were 7 patients with mastoid and sinus or jugular thrombosis. Three of them recovered and 4 died, 2 from pneumonia.

There were 14 patients with postabortion or puerperal sepsis, with 9 recoveries and 5 deaths. Of the 5 that died 2 were moribund when transfused and 2 died of pneumonia. One of the latter had run a normal temperature for four days previous to onset of pneumonia.

Of the 6 remaining patients 1 with an empyema recovered; 1 starting with an influenza infection, with particularly bad tonsils, also recovered; 1 patient with osteomyelitis, and 1 with osteomyelitis combined with suppurative arthritis, recovered; 1 patient with a suppurative arthritis died; 1 died from endocarditis.

Our figures in this group then show 17 recoveries and 12 deaths, and of that 12, 2 were moribund and 1 had an endocarditis.

Our total figures are as follows:

Diagnosis.	Total.	Deaths.	Recoveries.
Mastoid cases	22	10	12
Malignant endocarditis	7	7	0
Postabortion and puerperal sepsis	19	9	10
Osteomyelitis	5	1	4
Miscellaneous foci	15	10	5
	68	37	31

This gives out of 68 patients 31 recoveries and 37 deaths, but of these 37 deaths 7 patients were suffering from malignant endocarditis and 4 others were moribund at time of transfusion. I feel that we had a fighting chance in only 57 patients, giving a ratio of 31 recoveries to 26 deaths, and of these 26 7 died of a complicating pneumonia and 5 of meningitis.

Conclusion. This report of our work on sepsis is not complete, but even this limited number of patients seems to me to show the efficacy of blood transfusion in this condition. I feel that a great many patients could be saved if transfusion were started early and given every forty-eight hours until the blood cultures became sterile and the clinical improvement sufficiently marked to make it safe to stop. In most instances it is best to give only 500 to 600 cc of blood—less in children. I usually withdraw from the patient one-half to two-thirds of the amount to be given just before starting the transfusion.

It is evident also from this report that the most dreaded complications are pneumonia and meningitis. Escaping these, and given a fighting chance, blood transfusion offers any patient with septicemia at least a 50 per cent chance for recovery.

BIBLIOGRAPHY.

1. Novy, F. G., and Dekrief, P. H.: Jour. Am. Med. Assn., 1917, **68**, 1524.
2. Drinker, C. K., and Brittingham, H. H.: Arch. Int. Med., 1919, **23**, 133.
3. Unger, L. J.: Jour. Am. Med. Assn., 1921, **77**, 2107.
4. Bernheim, B. M.: Jour. Am. Med. Assn., 1921, **77**, 275.

THE INTERESTING BEHAVIOR OF TUBERCULOUS GUINEA-PIGS UNDER PARATHYROID AND CALCIUM ADMINISTRATION; A PRELIMINARY REPORT.

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and

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When this work was started, in 1914,[1] it was rather generally felt that in the tuberculous individual there was a lessened calcium tissue content and that this was one of the underlying factors in susceptibility to the disease. This belief has been advanced and contradicted up to the present time, and though it is claimed by some recent investigators[2] that there is no such deficiency, count-

[1] Proceedings Philadelphia Pathological Society, 1915, **36**, 29; 1916, **37-38**, 29.
[2] Marvel and Wells: Am. Rev. Tuberc., 1923, **7**, 1.

less clinicians still urge the use of calcium in the treatment of the disease. Were we to rebuild the theory upon which this work was done to conform to present-day knowledge we would be prone to agree with their contention, but would feel that, though the cells of the body might be constantly bathed in fluids of normal calcium content, it was not even then proved that they were able to make proper use of the obtainable calcium. In other words, though you offered them the food they needed, you did not prove that it became a part of their intracellular chemistry.

Let us state in the beginning that the basis of our work was purely theoretical, and that we are herein briefly reporting the results of our investigations suggested by these theories. One theory was that there was some derangement of calcium metabolism, as the result of which it was not properly taken up and utilized by the tissue cells. It made little difference for our work whether this applied to all of the cells of the body or only to those that entered into the destruction of the tubercle bacillus.

It should be said that these thoughts came to one of us as the result of rather closely following the work of Russell,[3] based upon the lime-salt starvation theory. It will be recalled that this investigator, after an enormous amount of clinical work, summed up his experiences with the opinion that there was a systemic need for calcium, but for some reason there was a marked difference between calcium administration and calcium metabolism; that, though the substance was fed in large or small quantities, tuberculous subjects evidently lacked something that was necessary to cause it to enter into true intracellular chemistry.

Some years later it occurred to one of us that, as the parathyroid glands were evidently the controllers of calcium metabolism, the underlying factor might be a hypoparathyroidism; that in tuberculosis there was a lessened parathyroid secretion which prevented the absorbed calcium from taking part in the true action for which it was needed.

There has, of course, been much controversy upon the true function of these small glands, but their action in calcium metabolism seems well established. A recent editorial[4] crystallizes our knowledge upon the subject and leaves little doubt as to their importance in this regard.

With these two thoughts in mind it was determined to see if the administration of these two substances, separately and together, would in any way influence the course of tuberculosis in guinea-pigs. The results of our investigations herein given seem to warrant a continuation of this work, as well as to furnish sufficient justification for a thorough clinical investigation of the problem.

[3] Russell, John F.: Med. Record, 1909, **76**, 889 and 1021; 1911, **80**, 12. Van Gieson, I. and Lynah H. L.: Med. Record, 1912, **81**, 883.

[4] Jour. Am. Med. Assn., 1923, **31**, 663.

Stress of other work has taken both of us away from the subject for some time, and it is largely with the hope of stimulating such a clinical study that this purely preliminary report is made. It is our feeling that the work as it stands is only highly suggestive, but that in it somewhere possibly rests a truth of the greatest value to mankind. We can conceive of no danger to the patient in carrying out such clinical investigations. A very brief experience with the substances in 9 advanced cases of pulmonary tuberculosis in man showed such a striking change from the steady weight losses they were experiencing as to make us feel it a matter worthy of study by those better able to weigh the results than ourselves.

In carrying out our work we first took 7 guinea-pigs and placed them in separate cages in a quiet well-aired room. They were given all they would eat, and weighed once a week. When they began to show a steady weight gain they were deemed ready for inoculation. Due regard was paid to each factor that could interfere with the value of the experiments, so that they can be said to be influenced adversely by nothing but a minimum of excitement. One who carries out weight experiments upon these little animals will early observe that such a trifling thing as putting them into strange cages, or moving the cages to which they are accustomed to other parts of the same room, will cause them to lose weight. The same applies to excitement or handling, particularly those infected with tuberculosis.

As it was our desire to produce a tuberculosis that would more nearly approach the disease as generally encountered in human beings, we chose a greatly attenuated strain of the human tubercle bacillus. The particular strain used was a descendant of the Saranac culture of Baldwin, known as "R. I.," which had been subcultured in the laboratory of one of us (R. C. R.) since 1904. This strain was the one which Gardner[5] found to be of such low virulence that it produces "Lesions which progress to caseation, and that this caseation, together with the accompanying proliferation of fixed tissue cells, is then absorbed. The healing process is one of resolution, of which no trace remains at the site of the former lesion." Gardner's observations were upon the pulmonary lesions following inhalation inoculation. It is our observation that this course is rarely encountered following intraperitoneal inoculation. In fact, with the large doses used by us many massive lesions occurred, and when we doubled our dose, as we did in one group, the animals were overwhelmed by the infection. It is probably the case that the course of the lesions in untreated pigs is governed by the size of the dose and the varying susceptibility of the animals.

In our first two series of 7 animals each an intraperitoneal inoculation of 1 cc of a heavy normal salt suspension of the organism was

[1] Am. Rev. Tuberc., 1922, **6**, 163.

given. The medication was suspended in sterile distilled water, placed upon bread and given once daily as follows:

1. Tuberculous control.
2. Tuberculous, 1 gr. calcium lactate.
3. Tuberculous, $\frac{1}{80}$ gr. parathyroid substance (Armour & Co.).
4. Tuberculous, 1 gr. calcium and $\frac{1}{80}$ gr. parathyroid.
5. Non-tuberculous, 1 gr. calcium.
6. Non-tuberculous, $\frac{1}{80}$ gr. parathyroid.
7. Non-tuberculous, 1 gr. calcium and $\frac{1}{80}$ gr. parathyroid.

This was continued for a period of three and a half months. It was early noticed that the tuberculous pigs, with the exception of tuberculous control, ate more food than the well pigs, and it was shown by actual food-weighing that the tuberculous pig on both preparations consumed far more food than any of the others. Singularly enough, this was the case in each series of experiments. From our observations it would seem that one could safely say that a tuberculous pig receiving both drugs will eat more than any of his fellows in a like series, and that he will even eat more food than a normal animal living under like conditions.

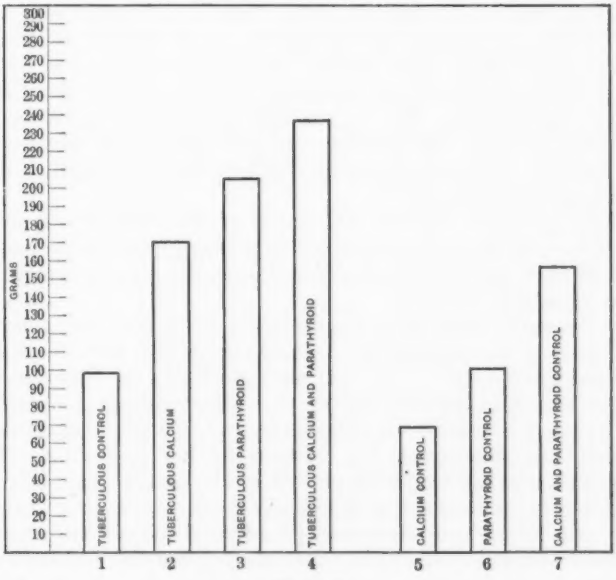

CHART I

In Chart I will be seen the result of our first series as regards ultimate weight gains. These results are remarkable from several standpoints, and gave much encouragement for further investiga-

tions. It will be seen that the tuberculous pigs gained more than the non-tuberculous, but that the order of gain was consistent in both.[6]

There is much of a suggestive nature in the autopsy notes regarding the extent of the macroscopical evidences of tuberculosis. They are briefly as follows:

1. Tuberculous control: Very large caseous mass in the omentum, two lesions 0.5 cm. in diameter in the liver and one in the anterior wall of the stomach. (These lesions were larger than the combined lesions of the other three pigs.)

2. Tuberculous calcium: Several small caseous masses in the omentum, two very small caseous nodules in the liver and adhesions between the liver and the belly wall.

3. Tuberculous parathyroid: Four small caseous masses in the omentum and several small nodules in the liver.

4. Tuberculous calcium and parathyroid: Small caseous button in belly wall at site of inoculation, a minute nodule in the liver with an adhesion between it and the small bowel. (All much smaller than in either of the others.)

Because of these results the experiment was duplicated in every particular with the results as seen in Chart II. With the exception of the tuberculous parathyroid pig there is a marked uniformity in the two results. This animal apparently enjoyed little native resistance to the disease, as he showed massive lesions, eventually dying of pneumonia. Pneumonia likewise killed the non-tuberculous calcium pig. The most remarkable feature was the weight gain of the tuberculous parathyroid and calcium animal, a gain which exceeded 270 gm.

From these two series it was apparent that there was a fairly constant ratio of weight gain upon the different types of medication in well pigs, and that there was little necessity of continuing the work upon these controls.

At the end of this series it was decided not to sacrifice the animals, but to see if the well pig upon the two drugs had been given any real resistance to the disease. It was accordingly inoculated as the others had been and allowed to go without further medication. With it were continued the tuberculous control and the tuberculous calcium and parathyroid pig without further medication. The weight gains in nineteen-week periods will be seen in Chart III. It is extremely interesting that at autopsy the first-mentioned of these three (the former non-tuberculous parathyroid and calcium) showed no macroscopical evidences of tuberculosis. For this we could not account at the time, but it is possibly in conformity with Gardner's findings. If so it is the only evidence in the group of the entire

[6] For the average weight gains of well guinea-pigs based upon 3634 investigations, the reader is referred to Wood's Reference Handbook of the Medical Sciences, 2d ed. **4**, 421.

disappearance of lesions. Whether or not its course of medication prior to inoculation was the cause of its entire recovery from the large dose of tubercle bacilli, it is of course impossible to say. It is, however, worthy of remark that this was the only animal in which it occurred.

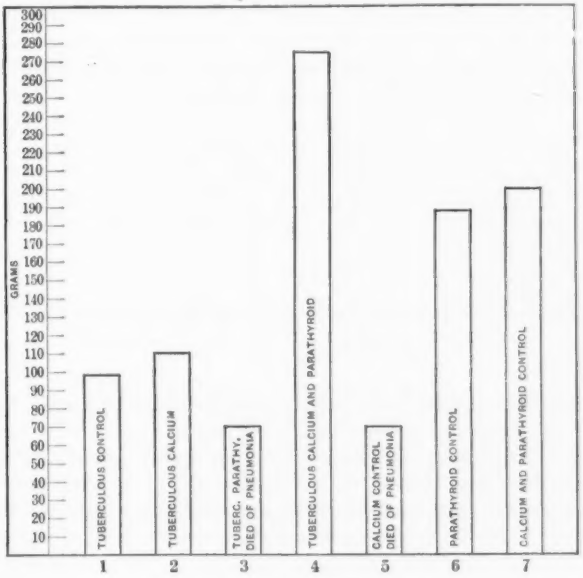

CHART II

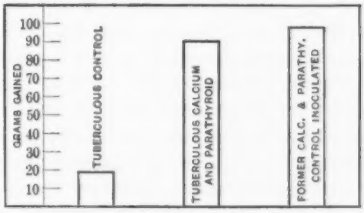

CHART III

Another larger series, consisting of 3 tuberculous controls and 20 tuberculous parathyroid and calcium pigs, was then started. Shortly thereafter an epidemic of diarrhea broke out among them and carried off so many that the group was discontinued. They were carried along for such a short time as to be of little value, but it is worthy of note that at the last weighing preceding the epidemic

the average gain of the control pigs was 72 gm. as against 92 gm. of the tuberculous animals receiving both substances.

Some time after this a fourth series was started in the private laboratory of one of us (P. S. P.), as it was not convenient to repeat it where the others were done. These animals were unwisely given a dose twice as great (2 cc) as that of the former ones. Due to this overwhelming dose, the initial weight losses were greater and more prolonged than in either of the other series. These animals died in a short while, but their weight trend, as seen in Chart IV, is somewhat suggestive of our former findings.

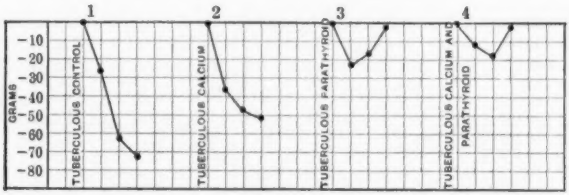

CHART IV

As has been stated, it was our hope to continue this work upon a larger and more conclusive scale, but stress of other duties has prevented our doing so. We do not feel that we have proved that our theories are facts, but we do feel that much of an extremely suggestive nature has been brought out and that, considering the vagaries of the laboratory guinea-pigs, there has been striking uniformity in the findings. This, together with a very brief and limited clinical trial, makes us feel no hesitancy in making a plea for a more extended trial under the auspices of those doing clinical work in this disease.

Summary. 1. The theory upon which these experiments were based is that in the tuberculous and those predisposed to tuberculosis there is a hypoparathyroidism which curtails the final stages of calcium metabolism, as the result of which the calcium does not enter properly into true intracellular chemistry.

2. Tuberculous and non-tuberculous guinea-pigs were given calcium and parathyroid substance separately and combined and, while it is not felt that the thesis is in any sense proved, it is deemed that the results are of such a suggestive nature as to warrant this preliminary report.

3. The results so far can be briefly summarized as follows:

(*a*) The lesions were greater in the tuberculous control and less marked in the calcium-fed animals. In those given parathyroid and in those getting both substances the lesions were still less marked.

(*b*) The weight gains bore an inverse relation to the size of the

lesions, as would be expected, and were much greater in those upon the combined medication.

(*c*) The tuberculous animals receiving both drugs ate far more than either of the others and even more than normal pigs under like conditions.

(*d*) It would seem that if one wished to make a guinea-pig gain enormously while taking calcium and parathyroid he should inoculate him with tuberculosis.

(*e*) The results in all of these series are as consistent as one who has handled laboratory guinea-pigs very much would expect, and make it highly suggestive that similar results might be obtained in certain classes of patients with tuberculosis.

4. It is our hope that others will take up this work in human beings for in it somewhere, we feel, is the answer to a problem that has baffled us all and that tuberculin has never answered.

THE SELECTIVE ACTION OF THE SUPRARENAL CORTEX SECRETION ON MESOTHELIAL TISSUES.

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In this article the clinical and embryological evidence supporting the following conclusions will be presented:

1. The suprarenal cortex secretion has a selective action on mesothelial tissues.

2. The normal development and continuous normal functioning of the sexual glands and skeletal muscular system is dependent upon the normal functioning of the suprarenal cortex.

3. Anterior cerebral defects include the pituitary gland, which in turn are accompanied by suprarenal cortex defects.

In a previous communication I[43] made the observation that the individual endocrine glands exerted a selective action on certain tissues, and that this selective action was specific and correlated with the germ layer from which the tissue in question was derived.

The work on the suprarenal cortex in recent years has strengthened my opinion that the cortex secretion is essential for the development and normal functioning of the mesothelial tissues. Since the suprarenal cortex and the reproductive organs have the same embryological origin, and since tumors of the cortex are frequently associated with sex anomalies, it was natural for workers in this field to try to demonstrate a functional relationship between these tissues. So far as I am aware no one has advanced the idea that the suprarenal cortex has a selective action on mesothelial cells.

To simulate diseased conditions of the suprarenal cortex by experimental methods proves a difficult task for several reasons, the principal ones being the anatomical fact that in higher mammals the cortex and medulla are so closely related and the apparently established physiological fact that the cortex is essential to life. No one can belittle the valuable contributions of the research worker in the field of endocrinology. For every statement made he demands an experimental demonstration. The clinician finds it easier to speculate and draw conclusions based upon clinical findings. But the clinician sees the lesions produced by so-called natural consequences, whereas the research worker sees lesions produced by means only simulating actual diseased conditions. This is particularly true in Addison's disease. The pigmentation of Addison's disease has not been successfully produced in animals by suprarenal extirpation. It is, of course, evident that the combined efforts of research worker and clinician are necessary for the advancement of endocrinology.

The interrelationship of the endocrine glands has made the problem a most difficult one. It is my opinion that the problem can be made easier by utilizing known embryological facts. In addition to the experimental data, it would seem worth while to study the clinical physiology of the suprarenal cortex in its relation to the embryological origin of certain tissues, such as mesothelial tissue.

It was stated in the aforementioned communication that pathological changes in the pituitary, *per se*, constantly produce changes in the bones, cartilage, fat, bloodvessels, lymph glands, smooth muscles and other mesodermal structures. Recently Bauer, in studying the pathological changes in osteogenesis imperfecta noted "That all mesenchymal tissues, such as bone, cartilage, vessels, hemopoietic organs, were affected. Chondrodystrophy and the progressive muscular dystrophies are other examples of affections limited to mesodermal structures. Schaeffer, independently of Bauer, found analogous affections of the ectoderm in amaurotic idiocy and hereditary spinal spastic paralysis."

The present article deals only with the suprarenal cortex and the selective action of its secretion on mesothelial tissues. The somatic and splanchnic layers of the mesoderm form on their celomic surfaces a single layer of squamous cells, termed the mesothelium. The mesothelium is, therefore, a differentiated part of the mesoderm. From the mesothelium are derived the following tissues: 1. Peritoneum. 2. Pleura. 3. Pericardium. 4. Urogenitals: (*a*) Wolffian body; (*b*) kidney (non-mesenchymal portion); (*c*) ovary; (*d*) oviduct: (1) Uterus (non-mesenchymal portion); (2) vagina. 5. Striated muscles: (*a*) skeletal; (*b*) cardiac.

The suprarenal medulla and cortex have different embryonic origins—the former is derived from the sympathochromaphil tissue of the ectoderm and the latter from the celomic epithelium of the

mesoderm. The cortical cells appear before those of the medulla and the cortex is already a large body before it receives the anlage of the medulla.

A study of the literature, and particularly that of recent years, convinces one that the suprarenal cortex, and not the medulla, is essential to life. Houssay and Lewis[31] established certain definite facts from their experiments with suprarenalectomy. Some of these facts are:

"1. Double suprarenalectomy is fatal in most species.

"2. Dogs survive extirpation of all chromaphil tissue contained in the suprarenals, when the remaining cortex is in good state.

"3. If the remaining cortex is removed the animals die, as after double suprarenalectomy.

"4. Dogs without the suprarenal medulla maintain their function normally.

"5. No abnormal pigmentation or asthenia is observed."

Biedl,[7] after an extensive study of the literature and analysis of the reported experiments on suprarenalectomy, as well as having performed a number himself, concluded that the suprarenal cortex is essential to life. Those animals which survived total extirpation of both suprarenals were shown to have accessory suprarenal tissue composed of cortical substance. Wheeler and Vincent[55] destroyed all the medullary tissue of the suprarenals by cauterization and left the cortical substance intact. Those animals in which considerable damage had been done to the cortex died. Hartman[28] is of the opinion that of the two suprarenal tissues, medulla and cortex, the latter is the more important and is essential to life. Crowe and Wislocki,[16] from their experiments on dogs, conclude that the suprarenal glands are vital organs, and it is probably the cortex which is essential to life, an opinion shared by the majority of workers.

Relation of the Suprarenal Cortex to Mesothelial Tissues. In order to avoid monotonous repetition, I will treat collectively the changes found in mesothelial tissues in those conditions which produce hypofunction and hyperfunction of the suprarenal glands, and also those changes produced by feeding experiments.

Hypofunction. Marshall and Davis[42] have shown that the excretory power of the kidney is very much reduced in animals in which the suprarenals had been removed. As this occurs despite the fact that the blood-pressure remains normal and the animals are in good condition, it would indicate that the suprarenals play an important part in renal activity. Bevier and Shevky[6] have also shown that extirpation of the suprarenals in rabbits decreases the excretion of urea. Cow[15] demonstrated that there was a direct vascular connection between the kidney and suprarenal, but this has not been demonstrated in man. Bremer[8] claims that the renal, suprarenal and sex-gland arteries are derived from an early periaortic plexus.

Addison's disease produces a hypoplastic or atrophic state of the

suprarenals. The kidneys are small and atrophic and chronic interstitial nephritis is frequent. Kyrle[25] found deficient spermatogenesis and degenerative changes in the interstitial glands in this disease. Impotency and amenorrhea are usually present. The extreme degree of muscular asthenia is one of the outstanding features of this disease. The cardiac muscle shares in this asthenia and is atrophic, thus accounting for the weak heart action and possibly the low blood-pressure.* Loss of epinephrin, through destruction of the medulla, cannot explain the low blood-pressure, because investigations have shown that circulatory blood does not contain enough epinephrin to influence the blood-pressure.

Biedl's extirpation experiments on the fish species, skates and rays, give very strong support to the opinion that the suprarenal cortex has a selective action on the skeletal musculature. In this species of fish the suprarenal medulla and cortex are anatomically separate. Excision of the interrenal (cortex) tissue produced striking symptoms. These, which began, as a rule, seven to eight days after operation, consisted of lessened movements and lifelessness. The spontaneous swimming around in the tanks became decidedly less. Fourteen to eighteen days after operation the muscular asthenia became so pronounced that the fish were unable to swim. They lay practically the whole day in a corner of the tank and took no nourishment. Stimuli failed to produce a reaction. Three weeks after operation they died with general prostration.

Elliott and Tuckett,[21] from their observations, concluded that the cortical portion has a definite relation to the skeletal musculature. Elliott, speaking of the muscle tone control says:

"The striped skeletal muscles form a homogenous group which is continually under a tonic influence. This tone is for the most part derived from direct nervous impulses, but the diseased state of myasthenia gravis proves that the tone is not altogether supplied from the central nervous system. Myasthenia might, in the skeletal muscles, correspond to the state of Addison's disease in the bloodvessels. But this is only a surmise. I have tried in vain to discover an active substance in the muscle plates of striped muscles. Professor Herring was also disappointed when he examined for this purpose the electrical organs of the skate, which are exaggerated motor plates."

Elliott and Tuckett noted that the suprarenals increase with the development of the skeletal muscles, the increase affecting mainly the cortex. They also found that the cortex parallels the weight, whereas the medulla remains stationary. Severe exhaustion is always associated with hemorrhagic dilatation of the blood spaces in the cortex. In the kitten a movement of fat from the outer to

* That the cardiac muscle atrophy may be due to the long-standing illness is a possibility, but this is unlikely when we compare it with the cardiac muscle found in other diseases of longer standing than Addison's.

the inner third of the cortex was produced by exhaustion. In a dog that had journeyed thirty miles all cortical cells were found to be vacuolized to a degree only seen in the fat-bearing zone of the outer third of the suprarenal cortex. In a study of the suprarenals of other animals it was found that the fowl medulla is very large and is three times that of the guinea-pig, which has comparatively the largest suprarenal cortex. It would seem that the lower the animal in the scale of vertebrates, the larger is the stock of chromaphil tissue.

The above-mentioned authors conclude that the following substances are evidence of secretory activity: (1) A fatty and (2) a doubly refractive substance; (3) brown granules of the cortex; (4) the chromaphil substance of the medulla.

The first two are nearly related. The doubly refractive substance increases with rest, when the fat becomes less abundant. In phases of exhaustion it vanishes and the fat spreads all over the cortex. But neither are essential factors in a generalized type of cortical activity, for neither appears in the sheep. The brown granules appear characteristically and plentifully in the guinea-pig and over a restricted area in the ornithorhyncus. They accumulate with rest and disappear very early in exhaustion; the cytoplasm of the cells in which they have been stored then develops fat. Exhaustion of the medulla is shown to be a progressive thinning of the substance, which stains yellow with potassium bichromate. In states of extreme exhaustion this stain finally vanishes.

It is true that epinephrin delays the onset of fatigue in skeletal muscles, but this is given off only in emergency periods, and my point is that the cortex secretion maintains the *normal* skeletal metabolism. Panella,[46] Cannon and Nice,[12] and Gruber[25–26] have demonstrated that epinephrin delays the onset of fatigue in skeletal muscles. Some (Hoskins, Gunning and Berry[30]) believe that the beneficial effect following epinephrin injections in muscle fatigue are due to circulatory improvement. Gruber believes that the improvement is not due to circulatory increase, but to overcoming fatigue products; for he demonstrated that epinephrin is beneficial even after denervation of the muscles, with the muscles in a state of dilatation. He likewise showed that epinephrin combats the effects produced artificially by injections of lactic acid and phosphate. Cannon's well-known work seems to prove that epinephrin is only present in the circulation during periods of great stress—the so-called emergency theory. There is some question, however, whether epinephrin represents the true principle of medullary secretion.

Bardier and Bonne,[3] in studying the modifications produced in the structure of the suprarenals by tetanization of the muscles, found that these affected the cortex of the gland, not the medulla. Vincent says "We do not know why its [cortex] removal causes

death, but it is possible that this is due to some defect in muscular metabolism."

Of lesser importance are the changes found in the peritoneum, pleura and pericardium in diseases of the suprarenals. Just what changes these tissues should show in diseases of the suprarenals is questionable. In Addison's disease there usually exists, and more particularly in the end stages of the disease the picture of peritonitis. The abdomen is retracted and the abdominal walls are tense, producing what Ebstein[19] termed "pseudoperitonitis." The peritoneum is smooth and glistening. Pleural and pericardial adhesions are a frequent finding.

In acute and chronic infections the lipoid content of the suprarenal cortex disappears, whereas in chronic circulatory diseases it increases. Chronic nephritis falls in the latter group and, therefore, it is of interest to note MacCallum's[38] statement: "Rather curious is the frequent occurrence of pericarditis in the terminal stages of chronic nephritis, and in those cases it is generally difficult to find any bacteria."

Hyperfunction. Hypernephroma of a hyperfunctionating type produces marked changes in the urogenital and skeletal muscle systems. Female infants with this type of hypernephroma menstruate, and are unusually muscular and strong. Infant boys have premature development of the genitalia, and are equal in size and strength to boys at the age of fifteen and sixteen years. The literature contains many reports of cases of this nature. Glynn[24] gave a very good summary of the reported cases at the time his paper was written. He is certain that there is an intimate connection between sex characteristics and the suprarenal cortex. Bullock and Sequeira,[11] Apert,[2] Quinby,[48] Jump,[32] Strauch[51] and many others have reported cases. It is not necessary to go into detail regarding these cases, as the association between suprarenal cortex tumors and precocious sexuality is well known.

Pseudohermaphroditism is frequent associated with hyperplasia of the suprarenal cortex. Marchand,[40] who first reported such autopsy findings, found colossal hyperplasia of the cortex associated with a large accessory suprarenal.

Jump[32] says that at present we are justified in believing virilism and hirsutism are caused by increased functioning of the suprarenal cortex, varying in degree and due in some instances to hypernephromatous growth of the suprarenal cortex.

Vincent[54] concludes that there is considerable evidence which indicates that the suprarenal cortex has important functions in connection with the development of the reproductive organs. He says that tumors of the cortex are frequently, though not constantly associated with sex abnormalities. This is true, but tumors are not all of the same type and do not necessarily increase cortex function; in fact they may lessen its function.

Hyperplastic changes are found in the suprarenal cortex during rut or in pregnancy (Guieyesse,[27] Stoerk and von Haberer[52]). Aichel[1] noted that the suprarenals were large when the sex organs were well developed and during the breeding season. Stilling[50] also noted suprarenal enlargement in male rabbits during breeding season. Leupold[36] found a close relationship existing between the suprarenals and testicles. He says that when the suprarenals contain much fat the quantity of fat in the testicles is also high. The testicles contain less cholesterol than do the suprarenals, and when cholesterol diminishes in the testicles and the suprarenals it is generally first decreased in the testicles. He believes that this proves that the suprarenals have a higher function than the testicles. Podvissotzsky[47] and Mulon[45] called attention to the resemblance of the ovarian cortical cells to the suprarenal cortex. Mulon believes that the corpus luteum of pregnancy is a temporary suprarenal cortex. Elliott[20] says: "There is reason to believe that interrenal tissue is embedded in the sex gland itself, giving rise to lutein cells of the ovary or the interstitial cells of the testis. By the latter cells are determined the sexual character of the individual."

Serdioukov[49] carried out a series of experiments on pregnant and non-pregnant cats. These experiments showed that there exists a functional interdependence between the suprarenal cortex, the parenchyma of the corpus luteum and the interstitial gland of the ovary. They have a vicarious relationship. This conclusion is verified by the lipoid character of each of these tissues. Marassini,[41] Cecca[13] and others found an increase in weight of the suprarenals following castration. This affected only the cortex. The vicarious relationship may account for the cortical hyperplasia.

Feeding experiments with suprarenal substance also gives evidence of a relationship between cortex and sexual glands; van Herwerden,[53] using 1 or 2 mg. of dried suprarenal cortex tissue added to 10 to 15 cc of hay infusion containing Daphnia pulex, stimulated growth and accelerated the maturing and reproductive processes. Similar stimulation of growth was observed with the eggs of the snail and with frog larvæ. R. G. and A. D. Hoskins,[29] experimenting with white rats, fed them desiccated suprarenal substance. Hypertrophy of the testes and ovaries was noted in several of the younger animals, although some of the controls also showed a similar hypertrophy. Vincent believes the latter experiments would prove more valuable if cortical substance alone were employed for feeding; furthermore the process of desiccation probably removes the important "lipoids" which might contain physiologically active substances.

Recently in a series of cases in which I thought suprarenal cortex secretion might be beneficial, viz, amenorrhea, muscular asthenia and 1 case of Addison's disease, I gave five hundred injections of a

suprarenal preparation.* This preparation consisted of an acetone soluble solution of suprarenal substance after the epinephrin had been extracted. It was, therefore, a suprarenal residue of the whole gland and was not absolutely epinephrin-free. The results were entirely negative.

In this same series of cases I fed over a thousand 5 gr. capsules of desiccated suprarenal substance. Beef suprarenal glands were cut in half and the cortex and medulla were grossly dissected from one another. The cortical portion was desiccated and prepared in the usual manner. Here, too, the results were absolutely negative. The case of Addison's disease showed a rather remarkable improvement of five weeks' duration. But as Addison's disease, like exophthalmic goiter, has periods of remission, and as no benefit was noted in the other cases, this improvement can hardly be ascribed to the cortex-feeding. Shortly afterward, despite the daily administration of 60 gr. to 80 gr. doses of the cortex substance, the patient died of exhaustion. Autopsy revealed atrophic suprarenals. No tuberculosis was present.

For reasons which will form the subject of another paper, it is my opinion that disease of the pituitary gland is always accompanied by disease of the suprarenal cortex. Primary lesions in the pituitary produce pathological changes in the suprarenal cortex. Briefly stated for the purpose of the present article, it is maintained that the posterior lobe of the pituitary gland has a selective action on mesenchymal tissues, of which the suprarenal cortex is a part.† The mesenchyme and mesothelium are differentiated parts of the primitive mesoderm, and are closely related. How closely related these tissues are is evidenced by the work of Lewis,[37] who says:

"The migratory mesenchymal cells in cultures of the embryonic chick heart show all stages of transformation from the bipolar and multipolar reticular cells to the flat mesothelial forms. One can actually observe this change in form. Such mesothelial cells seem to differ from the mesenchymal cells only in form and not in structure, indicating that mesothelium is to be considered not as a tissue differentiated from the mesenchyme, but merely as a change or transformation in form."

Further evidence of their close relationship is shown by Clarke's[14] experiments, which indicate that mesothelium can be formed from the mesenchyme, even in adult life.

If the posterior lobe of the pituitary has this selective action on mesenchymal tissues, such as bone, smooth muscle, connective

* This suprarenal material was kindly furnished me by the Research Department of Parke, Davis & Co.

† The well-known action of pituitrin on smooth muscle and bloodvessels is an evident clinical demonstration of its effect on mesenchymal tissues. From a speculative standpoint it might be theorized that the beneficial action of pituitrin in diabetes insipidus is due to its effect on the collecting tubules of the kidney, which are mesenchymal in origin.

tissues and bloodvessels; then it would be reasonable to suppose that the great increase in the weight of the bones, such as seen in acromegaly, requires a commensurate enlargement of striated muscle to control them. This is accomplished by suprarenal cortex hyperplasia. Falta[22] says that suprarenal cortex hyperplasia is a very frequent finding in acromegaly.

It is apparent, therefore, that disease of the posterior lobe of the pituitary gland will produce pathological changes not alone in mesenchymal tissues, but through accompanying cortical changes in mesothelial tissues as well.

It is of interest that injections of posterior lobe extract produce a hypertrophy of the suprarenal cortex. Sexual function in the early stage of acromegaly is increased. Great increase of muscular power in this stage is very apparent, these individuals posing in circuses as "strong men." The kidneys are enormously enlarged and show a true hyperplasia. In 2 cases of acromegaly Fischer[23] found immense suprarenals, affecting especially the cortex. Delille[18] likewise found this condition.

In hypoplastic states of the pituitary gland, hypoplasia of the suprarenal cortex is found. Total aplasia of the suprarenals is found in anencephaly, hemicephaly and other failures of brain development. Ziegler[57] cites several cases of anencephaly and hemicephaly associated with aplasia of the suprarenals. Zander,[56] Morgagni[44] and Czerny[17] also report brain defects associated with suprarenal aplasia. Kaufmann[33] says that the suprarenals and cerebrum have been placed in functional and genetic relationship. According to him, in hemicephaly and anencephaly the suprarenals are almost constantly found to be hypoplastic in greater or lesser degree. He quotes Zander to the effect that the suprarenals are hypoplastic only in defects of the anterior portion of the brain. From this it follows that the anterior cerebral defects include the pituitary gland, which would, therefore, account for the suprarenal cortex defect. Recently Büchler[10] tried to show a relationship between the pituitary and midbrain. Kohn[34] believes that suprarenal hypoplasia is secondary to changes in the hypophysis in anencephalic fetuses. Defects are found in the infundibulum and pars nervosa. The epithelial portion also show changes. There is scarcity of oxyphil cells and large basophil cells. Browne[9] studied 5 anencephalic fetuses. He was struck by the constancy with which the thymus, suprarenals and ovaries were involved in association with the anencephaly. Commenting on Browne's work, a leading article in the *British Medical Journal* (1920, **2**, 828) says: "The most rigorous search on the basis cranii of his anencephalic fetuses showed absolutely no trace of a pituitary gland. The syndrome, consisting of protruding tongue and eyeballs, nasal aquilinity, obesity, thymus hyperplasia, suprarenal and genital hypoplasia and stunted growth of body and limbs, agrees in the main with the

features of what are called hypopituitarism and apituitarism."* Barlow,[4] however, examined 4 anencephalic fetuses. He found no difficulty in locating the anterior portion of the pituitary gland. In none of them was there a real attempt at the formation of a sella turcica. He states that from the discovery of the anterior segment of the pituitary gland in 4 successive typical examples, it may be concluded that the other features of the condition are not due to apituitarism.

There can be no doubt, I believe, that defects of anterior portion of the brain involve the pituitary gland. But there also can be no doubt that the pituitary gland is not the etiological factor in the cerebral defect as Browne would prove, but is merely involved through its anatomical location. In Zander's 43 cases of anencephaly the suprarenal cortex defect was present only in those cases which included the anterior portion of the brain. We may conclude that in those cases of anencephaly which include the pituitary gland the suprarenal cortex is hypoplastic. It is apparent that some anencephalics do not have apituitarism and, therefore, do not show the syndrome completely. Barlow's 4 cases were probably of this type.

Mackenzie[39] says:

"The aplasia or hypoplasia of the glands [suprarenals] in conditions of anencephaly and similar defects of the central nervous system is well authenticated and is of much greater interest on account of the fact that a proper explanation of the changes in these conditions may ultimately lead us to a clearer view of the functions of the cortical portion of the glands."

The embryological idea expressed in this paper would seem to offer an explanation for a better understanding of the endocrine problem.

Summary. A review of clinical and embryological evidence supports the following conclusions:

1. The suprarenal cortex secretion has a selective action on the mesothelial tissues.

2. The normal development and continuous normal functioning of the sexual glands and skeletal muscular system is dependent upon the normal functioning of the suprarenal cortex.

3. Anterior cerebral defects include the pituitary gland, which in turn are accompanied by suprarenal cortex defects.

BIBLIOGRAPHY.

1. Aichel, O.: Vergleichende Entwicklungsgeschichte und Stammesgeschichte der Nebennieren, Arch. f. mikr. Anat., 1900, **56**, 27.

2. Apert, E.: La portion corticale de la capsule surrénale, ses relations physiologiques et pathologiques avec le cerveau et les glands genitales, Presse méd., 1911, **19**, 865.

* "Nature's Teratological Experiments".

3. Bardier, E., and Bonne: Note sur les modifications produites dans la structure des surrénales par la tétanization musculaire, Jour. de l'anat. et de la physiol., 1903, **39**, 296.

4. Barlow, D. L.: Apituitarism and the Anencephalic Syndrome, Brit. Med. Jour., 1923, **1**, 15.

5. Bauer, K. H.: Hereditary Constitutional Affections, Klin. Wchnschr., 1923, **2**, 624; Abstract, Jour. Am. Med. Assn., 1923, **81**, 172.

6. Bevier, G., and Shevky, A. E.: Urea Excretion after Suprarenalectomy, Am. Jour. Physiol., 1919, **40**, 191.

7. Biedl, A.: Innere Sekretion, Urban and Schwarzenberg, Berlin, 1910, pp. 141–147.

8. Bremer, J. L. (quoted by Dawson, A. B., and Reis, J. H.): An Anomalous Arterial Supply to Suprarenal, Kidney and Ovary, Anat. Rec., 1922, **23**, 161.

9. Browne, F. J.: The Anencephalic Syndrome in its Relation to Apituitarism, Edinburgh Med. Jour., 1920, **25**, 296.

10. Büchler, Paul: Hypophysis and Interbrain, Ztschr. f. d. Neurol u. Psychiat., 1922, **80**, 331.

11. Bullock, W., and Sequeira, J.: On the Relation of the Suprarenal Capsules to the Sexual Organs, Tr. Path. Soc. London, 1905, **56**, 189.

12. Cannon, W. B., and Nice, L. B.: The Effect of Adrenal Secretion on Muscular Fatigue, Am. Jour. Physiol., 1913, **32**, 44.

13. Cecca, R.: Ovar und Nebenniere, Soc. med. chir. de Boulogne, March, 1904.

14. Clarke, W. C.: Experimental Mesothelium, Anat. Rec., 1916, **10**, 301.

15. Cow, D.: The Suprarenal Bodies and Diuresis, Jour. Physiol., London, 1914, **48**, 443.

16. Crowe, S. J., and Wislocki, G. B.: Abdominal Chromaffin Body in Dogs, Bull. Johns Hopkins Hosp., 1922, **33**, 377.

17. Czerny, A.: Hydrocephalus und Hypoplasie der Nebennieren, Centralbl. f. allg. path. Anat., 1899, **10**, 281.

18. Delille, A.: l'Hypophyse et la modification hypophysaire, 1909, G. Steinheil, Paris, 352 pp.

19. Ebstein, W.: Peritonitisartiger Symptomencomplex in Endstadium der Addison'schen Krankheit, Deutsch. med. Wchnschr., 1897, **23**, 729.

20. Elliott, T. R.: The Adrenal Glands, Brit. Med. Jour., 1914, **1**, 1393.

21. Elliott, T. R., and Tuckett, I.: Cortex and Medulla in the Suprarenal Glands, Jour. Physiol., London, 1906, **24**, 332.

22. Falta, W., and Meyers, M. K.: The Ductless Glandular Diseases, Philadelphia, P. Blakiston's Son & Co., 1916, p. 351.

23. Fischer, B.: Hypophysis, Akromegalie und Fettsucht, Bergmann, Weisbaden, 1910.

24. Glynn, E. E.: The Adrenal Cortex, its Rests and Tumors; its Relation to the Other Ductless Glands and Especially to Sex, Quart. Jour. Med., 1911–1912, **5**, 157.

25. Gruber, C. M.: The Significance of Epinephrin in Muscular Activity, Endocrinol., 1919, **3**, 145.

26. Gruber, C. M.: Further Studies of the Effect of Adrenalin upon the Blood Flow in Muscles, Am. Jour. Physiol., 1918, **47**, 185.

27. Guieyesse, A.: La capsule surrénale chez la femelle du cobaye en gestation, Compt. rend. Soc. de biol., 1899, **51**, 898.

28. Hartman, F. A.: Endocrinology and Metabolism, New York, D. Appleton & Co., 1922, **2**, 105, 127, 237, 257.

29. Hoskins, R. G., and Hoskins, A. D.: The Effects of Suprarenal Feeding, Arch. Int. Med., 1916, **17**, 584.

30. Hoskins, R. G., Gunning, R. E. L., and Berry, E. L.: Effects of Adrenin on the Distribution of the Blood, Am. Jour. Physiol., 1916, **41**, 513.

31. Houssay, B. A., and Lewis, J. T.: The Relative Importance to Life of Cortex and Medulla of the Adrenal Glands, Am. Jour. Physiol., 1923, **64**, 512.

32. Jump, Henry D.: Clinical Syndromes Due to Suprarenal Diseases, Endocrinol. and Metab., New York, D. Appleton & Co., 1922, **2**, 345.

33. Kaufmann, E.: Spezielle Pathologische Anatomie, Berlin, George Reimer, 5 Auflage, 1909, p. 772.

34. Kohn, A.: Anenzephalie und Nebenniere, Deutsch. med. Wchnschr., 1922, **48**, 1666 (Secretary's Report, Verein deutsch. Aerzte, June, 1922).

35. Kyrle, J.: Ueber die Hypoplasie der Hoden in Jugendalter und ihre Bedeutung für das weitere Schicksal der Keimdrüsen, Wien. klin. Wchnschr., 1920, **33**, 185.

36. Leupold, E.: Beziehungen zwischen Nebennieren und männlichen Keimdrüsen, Jena, 1920, Gustav Fischer, 62 pp.
37. Lewis, Warren H.: Mesenchyme and Mesothelium, Jour. Exper. Med., 1923, **38**, 257.
38. MacCallum, R. G.: A Text-book of Pathology, 2d ed., Philadelphia, W. B. Saunders Company, 1922, 231 pp.
39. Mackenzie, J. J.: Endocrinology and Metabolism, Loc. cit, 1922, **2**, 257.
40. Marchand, F.: Beiträge zur Kenntnis der normalen und pathologischen Anatomie der Glandula carotica und der Nebennieren, Festschr. f. R. Virchow, 1891, **1**, 537.
41. Marrassini, A.: Sopra le modificazioni che si hanno nelle surrenali in rapporto con alcune variazioni della funzione e della funzione renale, Lo Sperimentale, 1906, **40**, 197.
42. Marshall, E. K., and Davis, D. M.: Influence of Adrenals on the Kidneys, Jour. Pharm. and Exp. Therap., 1916, **8**, 525.
43. Moehlig, R. C.: Ductless Gland-cell Control, monograph, published privately, January, 1918, 70 pp.
44. Morgagni: Epistolæ Anatomicæ, 20 *a*. Cited in Endocrinology and Metabolism, Loc. cit, 1922, **2**, 259.
45. Mulon, P.: Notes cytologiques sur le corps jauve de grossesse chez le femme, C. R. Assn. Anat. Suppl., 1909, p. 150.
46. Panella, A.: Action du principe actif surrénal sur la fatigue musculaire, Arch. ital. d. biol., 1908, **48**, 430.
47. Podvissotzsky (quoted by Vincent, S.): Loc. cit, p. 244.
48. Quinby, W. C.: A Case of Pseudohermaphrodism, with Remarks on Abnormal Function of the Endocrine Glands, Bull. Johns Hopkins Hosp., 1916, **27**, 50.
49. Serdioukov, M.: The Functional Relationship Between the Glandular Portion of the Ovary and the Adrenal Cortex, Abstract, Presse méd., 1922, **30**, 130.
50. Stilling, H.: Ueber die kompensatorische Hypertrophie der Nebennieren, Virchow's Arch. f. path. Anat., 1889, **118**, 569.
51. Strauch, A.: Sexual Precocity in the Male, Am. Jour. Dis. Child., 1918, **15**, 132.
52. Stoerk, O., and von Haberer, H.: Beiträge zur Morphologie des Nebennierenmarkes, Arch. f. mikr. Anat., 1908, **72**, 481.
53. van Herwerden, M. A.: The Influence of the Adrenal Cortex on the Growth and Reproduction of Lower Organisms, Proc. Konink. Akad. V. Wet., 1922, **33**, 1339; Abstract, Endocrinol., 1923, **7**, 323.
54. Vincent, S.: Internal Secretion and the Ductless Glands, 2d ed., New York, Longmans, Green & Co., 2d. ed. 1922, p. 93.
55. Wheeler, T. D., and Vincent, S.: The Question of the Relative Importance to Life of Cortex and Medulla of the Adrenal Bodies, Trans. Roy. Soc. Canada, 1917, **11**, 125.
56. Zander, R.: Ueber functionelle und kinetische Beziehungen der Nebennieren zu anderen Organen, speziell zum Grosshirn, Beiträge zur path. Anat. u. Physiol., 1890, **7**, 489.
57. Ziegler, E.: A Text-book of Pathology, 11th ed. (English), New York, William Wood & Co., 1908, p. 513.

EPIDEMIC DIAPHRAGMATIC PLEURODYNIA OR "DEVIL'S GRIP."

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In the *American Journal of the Medical Sciences*, November, 1888, William C. Dabney, published a report entitled "Account of an Epidemic Resembling Dengue which occurred in and around

Charlottesville and the University of Virginia in June, 1888." An excellent description of the clinical features of the disease is given. The characteristics of the disease in the reported epidemics of 1923 correspond closely with Dabney's description. Dabney differentiated the disease from malaria and dengue. He considered it epidemic but not contagious and states that he and a number of his colleagues who had abundant opportunity for observing this condition agreed that it was a disease with which they had not previously met and which had not been described. He states that on account of the agonizing pain on attempting to move or to draw a deep breath a patient had described the condition as "the devil's grip" and it was commonly called by this name in Rappahannock County.

During the summer of 1923 an epidemic occurrence of an acute febrile condition, characterized by severe pain in the epigastrium or chest, was reported to the State Board of Health of Virginia by Dr. Maude M. Kelly as observed by her in two counties in that State. A prompt investigation was made and a report was published[1] by Payne and Armstrong. The condition was designated by them as an epidemic transient diaphragmatic spasm, a disease of unknown etiology, epidemic in Virginia. Hanger, Jr., McCoy and Frantz,[2] published an article, An Epidemic of Mild Fever of Unknown Nature giving a report of 16 patients admitted to the Presbyterian Hospital in New York after June 6 of that year. They regarded this series of cases as representative of a fairly widespread epidemic, and commented on the discussion in the daily papers of a peculiar malady called "devil's grip" which was said to be prevalent in the New Jersey summer resorts at that time, and in which the symptoms and general characteristics were similar to those found in their cases. These writers designated the condition "epidemic pleurodynia" and considered that the syndrome constituted a clinical entity characterized by sudden onset, pain in the chest or epigastrium, fever of brief duration and a tendency to recrudescence on the third day.

During the latter part of the summer of 1923, the daily papers in the Middle Atlantic States referred frequently to the prevalence of "devil's grip" particularly in Virginia and in New Jersey and it must be concluded that this disease was widely prevalent at that time. The writer's attention was drawn to the condition by conversation with Dr. Charles H. Weber and Dr. William Drayton of Philadelphia in July of this year at which time this disease seemed to be prevalent in Philadelphia, and during the following month he saw a number of cases. The following cases are illustrative and seem to be typical.

[1] Jour. Am. Med. Assn., September, 1923, **81**, 746.
[2] Ibid., p. 826.

Case Reports. CASE I.—Miss M., aged twenty-six years, a nurse, was admitted to the Philadelphia General Hospital Infirmary July 27, 1924, complaining of severe pain in the back. She was apparently well until previous morning though she had been tired at night for a week. She thought that she had strained herself lifting a heavy patient. At 6 P.M., she had a temperature of 101° F., chill at 6.45 and great difficulty in breathing on account of pain with each breath, together with headache and general discomfort. The following morning was breathing easier but headache was very severe. No apparent gastrointestinal symptoms; pain in the lower chest anteriorly and posteriorly and tenderness along lower ribs is very marked.

Examination. Patient is very drowsy; pupils react; tenderness extreme below scapulæ on both sides, breathing causes pain; breath sounds normal, no rales or friction; heart normal size and position, rate 100 regular; abdomen shows slight general tenderness to deep pressure, no localized mass or tenderness; skin normal except for flush of cheeks.

July 28, 1924. During the day the temperature dropped to 100° F., pulse 100, respiratory 30. At 11 P.M., temperature 104° F., pulse 140, respirations 34, blood-pressure 124 to 70.

July 29, 1924. Patient generally feels much better, and is able to breathe without pain. Expansion good and equal, chest resonant, an occasional whistling rale, no friction sounds. There is frequency and irritation on urination.

In the afternoon the pain returned and at 4.30 A.M. the following morning had a chill and rise of temperature to 104° F. Dyspnea and pain became extreme and tenderness over the lower ribs was marked.

July 31, 1924. Much better today. Headache which has been very troublesome has disappeared. Knee-jerks which were absent yesterday are now present but very sluggish. No abdomen reflex or Achilles-jerk. Left pupil larger than right, both react. Pain still present about diaphragm on right and tenderness in back as before. There are no signs of lung involvement and no signs of intra-abdominal trouble. Temperature declined to 98° F., pulse 80, respiratory 24. Drenching sweat.

August 1, 1924. Not as well as yesterday. Epigastric and chest pain and tenderness. Pupils dilated, left more than right. Knee-jerks not obtained. At 2:30 P.M. a slight chill, temperature 102° F., pulse 100. On August 4 there was an exacerbation of pain and tenderness with no febrile reaction. There was marked sweating at night. The patient felt weak and faint and fell to the floor when attempting to walk. She was discharged August 11 and after ten days at home returned to duty. On September 4 she was seen and stated that she felt as well as usual. There was slight tenderness over the lower ribs on the left. No pain on moving or breathing.

The knee-jerks and Achilles tendon reflexes were active. While in the hospital, the erythrocytes numbered 5,030,000; leukocytes 8850 to 11,000. The percentage of the latter was: Polymorphonuclears 62, lymphocytes 28, transitionals 4, basophiles 2, eosinophiles 2. A careful search revealed no plasmodia or stipple cells.

CASE II.—Miss P., a young woman, a nurse, was admitted to infirmary at the Philadelphia General Hospital August 1, 1924, complaining of pain in the chest. She felt well until this morning when she had a chill of short duration about 7:30 A.M. and since then has had slight coryza and felt generally uncomfortable. No headache and no sore throat; no cough or expectoration, no gastrointestinal symptoms. Examination shows pharynx markedly infected and several blebs present. Chest and abdomen are normal, reflexes normal. (Pupil, knee-jerks and biceps). Temperature reached 103° F., pulse 130, respirations 40. Respirations very short and labored; patient irrational at times. Culture of pharynx was reported positive for Klebs-Löeffler bacillus. Subsequent cultures negative.

August 2, 1924. Better, temperature 99° F., pulse 100, respirations 24.

August 3, 1924. In the afternoon pain in the chest became acute with feeling of weakness. Knee-jerks very sluggish and difficult to obtain. Temperature 103° F.

August 4, 1924. Drenching sweat—temperature normal.

August 5, 1924. Severe headache and dizziness. Temperature 100° F.

August 6, 1924. Headache. Temperature 101° F.

August 8. Pain in chest. Temperature normal.

Discharged in good condition August 13.

Erythrocytes 4,090,000, leukocytes 11,800, polymorphonuclears 60; lymphocytes 34; transitionals 5; eosinophiles 1. Examination of the red cells by Dr. Small showed an organism described by him in another report (p. 570 this number).

CASE III.—C. C., this patient, on the sevice of Dr. John M. Cruice at St. Joseph's Hospital was not seen by me but is included because the blood was examined by Dr. Small at the Laboratory of the Philadelphia General Hospital. A chauffeur, white, aged twenty-two years, was admitted to St. Joseph's Hospital, August 71, complaining of pain in the abdomen and at the costal margins on both sides. The family history was negative. Previous medical history was negative. There was no friction sound found, but there was pain and tenderness in the right hypochondrium. Pain in breathing, no mention of cough. The temperature on admission was 103° F. This promptly dropped. There were three slight recrudescences of pain with very slight temperature and pulse elevation. The last recurrence was on the 22d. He was discharged August 24 in apparently good condition.

CASE IV.—A man aged twenty-eight years, salesman, had a sudden onset of fever with a chill August 24. He had an agonizing pain in the lower chest with each attempt to draw breath. Temperature was reported as 103° F. There was no cough. The next day he felt better but the following day was again worse. On the afternoon of the twenty-seventh he felt very well and went to work on the twenty-eighth feeling as usual except for slight pain in the lower chest when walking. By noon pain was exceedingly severe on breathing and the temperature had reached 103° F. Headache was severe and sweating profuse. He stayed in bed for a day following this and after that was apparently well.

In the household of this man, a child of seven years was suddenly seized with severe frontal headache and the temperature was found to be 104° F. There was no abdominal pain or tenderness. Vomiting followed an attempt to give a purgative dose. There was a remission in the temperature and another rise to the former level with increase in the headache. The total duration of the attack was forty-eight hours.

Two days later a sister of this child, aged five, had fever and frontal headache with a similar remission and a like duration of the disease. There was no history of dietary indiscretion and no abdominal pain in these cases. Chest pain and pain on breathing was not complained of. These cases do not appear to be typical of this condition as described, but appearing in the same household and following the other case in onset it seems probable that they were manifestations of the same infection.

Discussion. These cases are characteristic of this condition as described by Dabney and the later writers. During the past few weeks I have seen other cases and heard of many cases occurring in Philadelphia. In discussing this condition with many physicians during August, I have been surprised to find that a number of them had just seen patients with symptoms corresponding to this disease. In the latter part of August I was in the central part of Pennsylvania, at a summer resort, and in response to inquiry there, found that there was an epidemic disease prevalent among the native population, not the summer visitors, which from the description of the symptoms, appeared to be the "devil's grip." About 20 typical cases were seen there by Dr. Norman J. Taylor, of Philadelphia.

It is interesting to note that there have been three complete descriptions of epidemics published, two of them within the past year. Hanger, McCoy and Frantz emphasized their belief that this disease was prevalent to the degree when it must be considered epidemic in and about New York City only a year ago, the daily papers in the metropolitan section gave much space last year to the prevalence of this condition, but it still is not generally recognized. The physician should be on the lookout for these cases. They carry a fairly definite symptomatology but may be confused with pleuritis, pneumonia or acute intra-abdominal inflammatory conditions.

Clinical Course. The descriptions of the course and symptoms as given heretofore agree fairly closely. Typically the onset is sudden, often with distinct chill, the temperature is elevated, reaching from 102° to 104° F., and the pulse may be very rapid. It is slow in periods of comfort and is probably increased in rate by the effort to breathe. The pulse curve usually follows the temperature curve proportionately. Pain is the main symptom, occurring in the epigastrium or back or both, and in the lower chest. It is aggravated by breathing or by motion. It is increased during the febrile attacks and decreased as the temperature drops. It is so severe at times as to make breathing almost impossible. With this pain there is very marked tenderness. The tenderness may persist after the pain has disappeared.

Fever and pain come on together, and they diminish together. There may be only one attack, but usually there are recrudescences of pain and fever occurring between twenty-four and forty-eight hours apart.

Headache seems a usual symptom, coming on later than the chest pain. It is usually frontal, it may be severe and persistent. Profuse sweating is characteristic. It occurs late, independent of any rise in temperature.

Prostration is not marked as in influenza. While the temperature is elevated these patients look extremely ill and the pain is severe enough to cause some shock, but as soon as the temperature drops and the pain subsides, they feel surprisingly well.

There is an absence of signs of lung involvement and pleural frictions have not been heard. The knee-jerks may be diminished or lost during the acute stage of the disease but promptly return to normal.

The prognosis is good. Deaths are not reported. Tenderness may persist for some time and the severe cases may feel weak for a long time after the attack. As a rule recovery is prompt and apparently complete. It may be that the disease may show different manifestations in young children. The leukocyte and red cell counts and the urine analysis show nothing characteristic and blood cultures have been uniformly negative. Smears of the blood from 2 of the cases mentioned above were examined by Dr. Small and are the subject of a separate report by him (next page).

There have been no fatalities reported and of course no autopsies in cases of devil's grip. This condition is certainly due to an acute infection, and the recurrences seem like those of a protozoan infection. The pain is probably due to involvement of the diaphragm or diaphragmatic pleura. Tenderness persists in the region of diaphragmatic attachments. We have not studied the diaphragm movements during the acute pain but in fluoroscopic study of our Case I the diaphragm movements were normal and equal on the two sides five days after the last chill.

Quinin was used in treatment on account of points of similarity between this condition and malaria.

The term "epidemic diaphragmatic pleurodynia" seems to designate this condition satisfactorily. It is questionable whether there is an active inflammation of the diaphragm as the change from pain to comfort is so rapid. The severe headache and reflex disturbances noted indicate some degree of nerve tissue involvement by the toxin. The selective localization of the toxic action is very constant. The pain seems pleural, the localization is certainly about the diaphragm.

Summary. A disease with a definite symptomatology which was reported as epidemic in Virginia, New York and along the New Jersey coast last summer has been prevalent in Pennsylvania this summer. Areas of infection have spread. This disease is not as generally recognized as it should be.

The infecting agent has not heretofore been recognized. The disease seems to occur only during the summer months but as yet no insect has been demonstrated to be a carrier. The mode of transmission of infection has not been found.

A study of the red cells for a possible protozoan infecting agent has been made in the Laboratory of the Philadelphia General Hospital by Dr. James C. Small and the results of his study are the subject of the next report in this issue.

A PROTOZOAN ORGANISM WITHIN THE ERYTHROCYTES OF PATIENTS SUFFERING FROM EPIDEMIC PLEURODYNIA ("DEVIL'S GRIP").

(Preliminary Note.)

By James C. Small, M.D.,

PHILADELPHIA.

(From the Bacteriological Laboratory, Philadelphia General Hospital.)

The recent occurrence of epidemic pleurodynia ("devil's grip")[1] in Philadelphia[2] has furnished the opportunity for making a careful search for the etiological agent of this disease. In considering the clinical manifestations of the disease certain outstanding features have directed attention to the probability of its being caused by a protozoan organism, rather than by a bacterium. Among these may be mentioned: (*a*) An absence of leukocytosis during the height of the fever; (*b*) sudden decline of fever with cyclic recurrences, and the relative freedom from symptoms during the intervals; (*c*) the absence of inflammatory foci, (*e. g.*, upper respiratory or intestinal), which might account for the general symptoms; and (*d*) an increase of eosinophiles, most marked during convalescence.

Accordingly attention was directed to a study of blood smears. Specimens from two patients were available. The one a nurse (Miss P.) in the Philadelphia General Hospital, diagnosed clinically by Dr. Robert G. Torrey; the other a young man (C. C.) from the medical service of Dr. John M. Cruice at St. Joseph's Hospital. In the former patient 5 specimen smear preparations were made at intervals, during two days; in the other case they were made once only, five days after the onset, but at the time of a mild recurrence of the painful respirations. These preparations were stained with Wright's stain. The Sörensen phosphate solution mixture buffered at pH 6.6 was used instead of distilled water for diluting the alcoholic solution of the stain on the slide.

Specimens from each of the patients showed inclusions within the erythrocytes, which in their more mature forms are illustrated by the photomicrographs. Study of these has led us to believe that they are protozoa. This finding is presented at this time, with a full understanding of the incompleteness of the observations to date, for the purpose of bringing it to the attention of the medical profession in order that others who may have the opportunity might undertake painstaking search for these organisms.

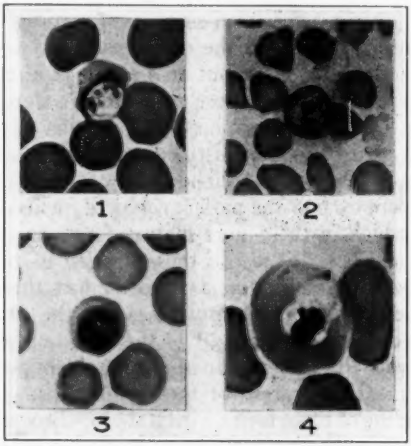
Since the finding of these forms within the erythrocytes of patients suffering from "devil's grip," we have studied preparations of the blood of normal individuals stained with the same solutions and by the same technic. Prolonged search has failed to reveal any inclusions, or any artefacts, which in any way bear a confusing resemblance to the forms mentioned.

The description of these organisms may be presented best by stating the findings in the serial smears of blood from the first patient (Miss P.)

Preparation No. 1, 11.30 A.M., *August 5* (*Miss P.*). The great majority of the erythrocytes appeared normal. A few erythrocytes showing pronounced basic stippling were found. Within certain erythrocytes there appeared small round or oval bodies, usually located eccentrically. They stained a brilliant blue throughout, sometimes with a single red chromatin granule. Little internal detail could be distinguished. The smallest appeared about half the size of a blood platelet. They were easily differentiated from blood platelets, even when the latter appeared superimposed upon an erythrocyte, by their brilliant blue staining as contrasted with the violet staining of the latter. Save for the presence of the inclusion the erythrocyte appeared normal.

Preparation No. 2, 4.00 P.M., *August 5* (*Miss P.*). Here again an occasional stippled cell appeared among the great mass of normal erythrocytes. The round or oval bodies appeared larger, occupying roughly from a fifth to a third of the enclosing erythrocyte. These erythrocytes did not appear swollen, nor did the remaining body appear differently from that of normal adjacent erythrocytes. The

staining again was a brilliant blue. Throughout there appeared threads of dark-staining material which with proper lighting showed a red tinge. These were arranged in a loose skein-like formation or without order.



Plasmodium pleurodyniæ within erythrocytes; Wright's stain.

FIG. 1.—Miss P.; 9:30 A.M., August 6, 1924. × 1200.
FIG. 2.—Miss P.; 12:45 P.M., August 6, 1924. × 800.
FIG. 3.—Miss P.; 7:20 P.M., August 5, 1924. × 1200.
FIF. 4.—C. C.; August 22, 1924. × 1600.*

Preparation No. 3, 7.20 P.M., *August 5* (*Miss P.*) (photomicrograph No. 3). Stippled cells were not found. The only abnormal erythrocytes appearing in this preparation were those containing the organisms, which now appear larger in size, so that they occupy the larger portion of the enclosing erythrocyte. There now appears a more definite arrangement of the inner blue mass and the differentiation of a narrow, clear, faintly blue tinged outer zone. Toward one side appears an irregular compact mass of the deeply staining material and several scattered small rod-like particles of the same material. The erythrocyte may or may not appear swollen. In either case a narrow outer zone of the erythrocyte alone remains, which may appear normal, or may be basophilic. Nothing resembling Schüffner's dots has been observed, neither at this stage, nor in the later preparations.

Preparation No. 4, 9.30 A.M., *August 6* (*Miss P.*), Fig 1. In these preparations only the erythrocytes containing the organisms appear abnormal. The organism occupies a large portion of the erythrocyte and maintains a round or slightly oval outline. It is less rich

* Photographs of these preparations showing greater detail and of other phases will be furnished by the author on request.

in the material staining deep blue and this material appears arranged in small round dotlike bodies, which lie scattered irregularly within a pale blue transparent body of the inclusion. This type is shown in photomicrograph No. 1.

Preparation No. 5, 12.45 P.M., *August 6* (*Miss P.*) (Fig. 2). The organisms found in this preparation presented practically the same characters as those found in preparation No. 4. Photomicrograph No. 2 shows one of these in which the large part of the inclusion is made up of the transparent, faintly blue tinged substance with a compact mass of the dark staining material and several scattered particles of the same. It will be noted in the particular one shown in photomicrograph No. 2 that the erythrocyte is considerably swollen. The narrow zone of the red cell surrounding the large organism shows basophilic staining. An erythrocyte "shadow" appears nearby, which probably represents the distorted remains of a cell, in which a parasite had reached maturity. In this preparation similar "shadows" were found with some degree of frequency.

A parasite from the St. Joseph's Hospital patient (C. C.) is shown in photomicrograph No. 4. Others found in the same smear appeared in different stages of development. The striking feature in this instance was the finding with considerable frequency of erythrocytes containing large clear rounded spaces which appeared as vacuoles. These corresponded in size and general contour to the spaces occupied by the larger organisms described above, and did not resemble anything previously seen in stained smears other than in this disease. Distorted erythrocyte "shadows" were also found. It is probable that both of these findings represent erythrocytes from which mature parasites had escaped.

Summary. It is believed that in one patient (Miss P.), where a series of examinations were made, different stages in the cycle of development of a parasite have been observed. The evidence is incomplete, but a striking resemblance to the developmental cycle of the malaria parasite is suggested by our study. The organism is protozoan, but differs from the malaria group in staining characters, in its morphology and in its lack of a destructive action on the contiguous portion of the erythrocyte enclosing it, since where only narrow peripheral zones of the erythrocyte remain, they may yet appear normal in their staining reactions. Pigment granules have not been observed.

In view of these findings the organism is believed to be a heretofore undescribed plasmodium and it is suggested that it be designated *Plasmodium pleurodyniæ*.

REFERENCES.

1. Dabney, Wm. C.: Am. Jour., Med. Sci., 1888, **96**, 488.
Payne, G. C., and Armstrong, Charles: Jour. Am. Med. Assn., 1923, **81**, 746.
Hanger, F. M., McCoy, C. C., and Frantz, A.M.: Jour. Am. Med. Assn., 1923, **81**, 826.
2. Torrey, Robert G.: Am. Jour. Med. Sci., This issue, 1924, **168**, 564.

THE SURGERY OF PULMONARY TUBERCULOSIS.

By John Alexander, M.A., B.S., M.D.,
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(*Continued from July, August and September,* 1924)

Sultan extracts an average of 20 to 30 cm.; once he was able to get only 8 to 12 cm. before it broke; once he extracted 41 cm. Not infrequently the stump of the accessory phrenic may be identified on the extracted main trunk, of which it is about one-quarter to one-third the size.

It is known—the original work has recently been painstakingly confirmed by Felix—that the phrenic carries no centrifugal pain impulses. Manipulation of it will, however, sometimes cause the patient severe pain in the chest and in the region of the diaphragm; the chest pain is the result of direct mechanical irritation of the mediastinal pleura by the phrenic nerve, and the diaphragmatic pain results from a cramp-like contraction of that muscle. This pain, or pain in the neck, may be so severe as to require the surgeon to abandon the radical operation. If he has succeeded in extracting as much as 10 cm. of the nerve, it is probable that he has ruptured the accessory phrenic, if present.

There are certain possible dangers of this operation of exæresis: (1) Hemorrhage from the phrenic artery or veins into the phrenic sheath, the blood appearing at the neck. Sultan saw no bleeding in 44 cases; Felix once saw trivial bleeding, easily checked. (2) Hemoptysis, perhaps from an adherent phrenic nerve tugging at infiltrated lung tissue as the twisting proceeds. Zadek saw this twice, but the final results were good; where there is history of hemoptysis he now twists the nerve very slowly. (3) Goetze has seen a cold abscess follow exæresis because the nerve was imbedded in a caseous focus. Sauerbruch would not do this operation in the presence of a tuberculous empyema, or if pleural adhesions were known to exist over the nerve, as the freeing of infectious material might cause a fatal mediastinitis. (4) The twisting may cause reflex cardiac and respiratory disturbances. This occurred in one of H. Alexander's cases, and he was obliged to interrupt the operation. Zadek and Felix have each seen temporary heart and respiratory stoppage. Dyspnea, rapid or slow, weak and irregular pulse are usual during the actual twisting of the nerve. Exæresis has been used extensively in a number of clinics, and no fatal results have been reported, Baer has used it 100 times without mishap; Felix knows of 240 cases (150 of them from Sauerbruch's Clinic) in which it has been performed without accident. It will probably become the operation of choice whenever maximum diaphragmatic paralysis is indicated.

Results of Phrenicotomy Used as an Independent Procedure. Of 60 simple or radical phrenicotomies performed at Sauerbruch's Clinic, 17 showed marked improvement before the supplementary operation was performed. As phrenicotomy produces only partial rest and lung compression, early favorable results often are not lasting; supplementary operations are demanded, as a rule. H. Alexander reports 13 of Sauerbruch's and Schreiber's patients, 12 of whom had bilateral disease and were too sick for a primary thoracoplasty, and 6 of them were too ill for artificial pneumothorax; of these 13, 6 were much improved, 3 slightly improved, 4 not changed. Pribam reported 5 good results: (1) A hemoptysis of three months duration was checked in six weeks and a severe right-sided disease arrested (operation recent); (2) and (3) were huge hemorrhages, and were checked completely; (4) improved enough for thoracoplasty, as were cases (2) and (3); (5) disease of twelve years' duration, very sick and phrenicotomy a last resort, much improved. Sultan reports 12 cases of exæresis used as an independent procedure: 2 patients apparently cured; 5 much improved; 5 unchanged. Fischer did Goetze's radical phrenicotomy upon 17 patients whom he traced from four months to two years later: 7 were cured, 9 much improved and 1 had progress of disease in the better lung. Sauerbruch believes that these must have been only early, and not advanced tuberculous disease. Goetze reports the disappearance of a cavity in midlung after radical phrenicotomy. Frisch and Fischer have used phrenicotomy alone with success in acute disease; Frisch reports a case of "galloping consumption" with fever of 39° to 40° C. and with two cavities in the right upper lobe. After phrenicotomy the temperature became 37.5° C. the sputum was greatly reduced, and with only a few tubercle bacilli. He has seen similar results in other cases. He also reports a case of hemoptysis, apparently being caused by an adhesion between the lung and diaphragm in an otherwise satisfactory pneumothorax, checked by radical phrenicotomy.

Because of the simplicity of the operation and of the excellent immediate results it is certain that radical phrenicotomy will soon be extensively used preliminary to artificial pneumothorax, and thoracoplasty. Because by itself it is rarely able to effect permanent improvement or cure, the temptation should be avoided of using it, because of its simplicity, without intending to supplement it at the proper interval with pneumothorax or thoracoplasty; to do so, and to wait for months in the hope of further improvement, may mean loss of the opportunity to carry out one or the other of these effective measures because of the appearance of active, progressive disease in the better lung.

Tuberculous Cavity of the Lung. Occasionally tuberculous cavities close spontaneously, but this is exceptional; after compression therapy it is the rule. A great majority of patients who have had thoracoplasty had cavity formation.

Soft-walled cavities are usually easily collapsed by a good pneumothorax or a complete thoracoplasty, but stiff-walled cavities may require one or more supplementary operations, which however, should not be performed for at least six months—until the thoracoplasty has been given every chance to obliterate them.

Paravertebral thoracoplasty should invariably be the first operation performed, and when the cavity is large or multiple or stiff-walled, a parasternal thoracoplasty should be added three weeks later. The two modern supplementary operations are extrapleural pneumolysis, and cavity drainage. The added compression of a firm "fill" after pneumolysis is very often able to cause the cavity wall to "give;" Sauerbruch, who uses a tight gauze tampon, has found that this most frequently occurs on the tenth day. In cases of bilateral cavity, in which the tuberculous disease has become inactive, and where there is a marked shrinking tendency, Sauerbruch and L. Spengler would perform bilateral extrapleural pneumolysis without preliminary thoracoplasty.

When none of the above mentioned operative measures have succeeded in collapsing a cavity, and when its contents are secondarily infected and draining poorly and causing symptoms of sepsis, and when the tuberculous disease is regressant, cavity drainage may be indicated (Sauerbruch, Jessen, Stöcklin, Wagner and Wilms). When these special indications are not strictly observed the results are likely to be very poor.

Sauerbruch was led to advocate drainage by having seen some cases do well after a paraffine "fill" or gauze tampon had ruptured into a cavity and caused spontaneous drainage (before opening the cavity the surgeon must assure himself that the free pleural cavity is walled off by adhesions). At present he sometimes attempts to obtain opening into the cavity in this way, if he fears that it might be difficult to locate it with the cautery; when using this method, sometimes he pares away a part of a greatly thickened pleura, or of a very thick cavity wall (after incision of the lung parenchyma), prior to placing the gauze tampon. Unless the cavity is very near the anterior chest wall, Sauerbruch prefers the posterior route, and never uses the axillary route.

After resection of sufficient lengths of two or three ribs the lung is freed from a few of its pleural adhesions for orientation, and entrance gained to the cavity with a thermocautery (Sauerbruch), or with a knife (Jessen). The retained secretions are scooped out and the cavity "saucerized" and packed with gauze. Jessen would doubly ligate and divide any bands stretching across the cavity. Packing is renewed until the cavity has filled with granulations and become obliterated. A bronchocutaneous fistula usually remains, and frequently may be closed by a musculocutaneous plasty after excision of the mucous membrane in the mouth of the fistula; this plasty should not be performed until at least six months after drainage was instituted.

Sauerbruch reports 18 cases where he followed his advocated sequence, that is, thoracoplasty, pneumolysis and gauze tampon drainage; among them were: 1 early death; 3 deaths after one and a half to three years from progression of tuberculosis in the originally better lung; 8 cures; 6 spontaneous ruptures of cavities, and later healing, although 2 with fistula. One of these patients had had 400 cc of sputum and has now been well for five years. In addition, he reports 8 cases of primary drainage without preliminary thoracoplasty or pneumolysis; of these, 2 died early; 2 improved but retained fistulæ; 4 were much improved, but with fistulæ. Baer reports 3 good results out of 4 large, stiff-walled cavities. Sonnenburg drained 5 patients, and "healed" 3 of them.

The earlier reported results of cavity drainage were very poor; it is only fair to say that no such rigid indications and contraindications were followed then as now. Ten years ago Tuffier and Loewy collected 45 cases; of them 17 died within three months and only 2 were cured. Landerer collected 19 cases: some were temporarily improved, but all died. Landerer "failed" in 3 cases, but none had had preliminary thoracoplasty. Rieckenberg cites a case of honey-combed cavity which was drained through a wound that measured 8 by 4 cm.; the patient could not expectorate well as the force of the cough was expended through the bronchus and drainage wound, and one day he suffocated by drowning in his own secretions. Drainage is contraindicated for multiple and honey-combed tuberculous cavities.

Tuberculous Empyema. Tuberculous empyema is usually secondary to a pulmonary tuberculosis, and often follows the direct rupture of a tuberculous cavity or tubercle into the pleural cavity. Not infrequently it develops from a serous tuberculous effusion that may have arisen during the course of artificial pneumothorax therapy. Empyema secondary to pulmonary tuberculosis is a grave complication and demands rare judgment in treatment.

Effusions may be divided into three main types: (1) Clear serous, with few cells; tubercle bacilli may or may not be found by smear, but are usually found by guinea-pig injection. Onset gradual or sudden, usually moderate fever and absorption in a few weeks; (2) purulent, turbid fluid, with fibrin and many cells and tubercle bacilli, but no pyogenic organisms; stormy onset, high fever, and spontaneous absorption may take place only after many months, or not occur at all; (3) mixed infection with pyogenic organisms; tubercle bacilli may be difficult to recover; diagnosis of tuberculosis may depend upon microscopical examination of a piece of pleura (excised at the time of thoracotomy, which may prove necessary). Tuberculosis may be the underlying infection, even if a pure culture of staphylococcus or pneumococcus is recovered. Mixed infection may occur from a needle puncture (it has been shown experimentally that artificial pneumothorax reduces the resistance of the pleura to infection), or as a metastatic localization of a general

infection, as an influenza, angina, and so forth, or as a result of spontaneous pneumothorax or of rupture of superficial tubercles or cavities during attempts to stretch firm adhesions with high gas pressures in artificial pneumothorax. The mixed infection in this last group is very virulent, and the outcome usually rapidly fatal. When the pleura is much thickened, and the clinical signs of infection are less marked, and the general condition of the patient permits, attempts should be made to kill the pyogenic organisms with antiseptic irrigations by the closed method.

The keynote of treatment is never to institute open drainage of a tuberculous empyema unless it is certain that the secondary infection is uncontrollable by other means. Main reliance is to be placed upon spontaneous absorption or repeated evacuation by aspiration, with or without antiseptic irrigations, and with or without air replacement.

Group (1) effusions (serous) rarely call for any treatment; in case they increase to such dimensions as to cause distressing symptoms from pressure on the mediastinum, heart or stomach, or from encroachment on the opposite lung, partial aspiration would be indicated. To withdraw a little of an effusion sometimes invites spontaneous absorption, but to withdraw all invites prompt recurrence.

Group (2), turbid, purulent effusions without pyogenic organisms, and those cases in group (3) in which the secondary infection does not demand open drainage, call for interference for the reason that these fluids tend to remain and leave chronic, infected empyema cavities, and that deposits of fibrin and organization of the sedimented debris tend to draw a lung, well compressed by artificial pneumothorax, out to the chest wall, and to check the gains that the compression may be making. Repeated partial aspirations may be carried out at whatever intervals the rate of reaccumulation may demand, and it is an almost invariable rule partially to replace the aspirated pus with air or nitrogen gas. Some of the effusion is always to be left in the chest because of its frequently favorable "sero-biologic" effect upon the tuberculous disease. Attempts to kill the pneumococcus and staphylococcus may be made with antiseptic irrigations of 1 to 5000 neutral acriflavine, or 5 cc of a mixture of iodin 1 gm., potassium iodid 2 gm., distilled water 40 cc, in 1000 cc water. Successes have been reported following aspiration of pus, and instillations of 1 to 3000 solution of gentian violet, or 1 to 1000 solution of acriflavin, or 5 per cent methylene blue, or Pregl's iodin solution (Stahl and Bahn), or 1 per cent formalin-glycerin solution (Kahn). Amounts of solution that will not cause marked rise of intrapleural pressure are allowed to flow by gravity through a needle, and then to escape, and this repeated until the recovered fluid is fairly clear, or two needles may be used and the fluid run in the upper one and allowed to escape from the lower one. It is very important that the gas pressure remaining in the pleural

cavity after aspiration be neither too high nor too low; manometer readings during the operation through a needle and tube that are free of fluid are necessary for satisfactory work. To attempt to regulate the gas pressure that is to remain after operation by the subjective symptoms of the patient and cough, is unsafe where a carefully graded lung compression is demanded on account of active pulmonary disease; too high a pressure encroaches upon the opposite lung and causes it to perform dangerous extra work; too little pressure allows the compressed lung to expand and may cause pain and undue dyspnea. At the end of the operation a slightly negative pressure should be left in order to allow for the possible rapid reaccumulation of the fluid. Appearance of a thoracic wall sinus at the site of needle puncture is not an unusual occurrence in these purulent tuberculous empyemata; it should be guarded against by using a narrow-gauge needle for all punctures and by injecting into it a few drops of iodoform-glycerin, or tincture of iodin, as it is withdrawn.

Extrapleural thoracoplasty is indicated for these cases, especially if complicated by bronchopleural or pleurocutaneous fistula, when repeated aspirations fail to obliterate the empyema cavity within a few months, else there is danger that secondary infection may occur (Hedblom), or that the patient may become so weak that an extrapleural or Schede thoracoplasty could not safely be undertaken (Levy). A day or two before operation most of the fluid is aspirated and air substituted, and the patient immediately examined with roentgen-rays to determine the extent of the cavity. The thoracoplasty is then performed in two or three stages, at intervals of two to three weeks, reaccumulated fluid being withdrawn one to two days before each operation. If fluid persists after the completed operation it should be aspirated or it may finally be necessary to perform open drainage and irrigations, and if this does not succeed in obliterating the remains of the cavity a small Schede operation (with primary skin closure—Hedblom) may be required. The Delorme-Fowler decortication operation should never be used on a tuberculous lung. The order of procedure just described is preferable to primary open drainage of the empyema cavity and secondary operations to obliterate it, as there is much less danger of infection of the thoracoplasty wounds. However, if the nature of the case demands immediate primary drainage, and if thoracoplasty is subsequently required to obliterate the cavity, every effort should be made to render the cavity and draining sinus as sterile as possible before making the large incisions for thoracoplasty. This sterilization (tubercle bacilli are not killed) is best accomplished with surgical solution of chlorinated soda (Carrel-Dakin), if bronchial fistulæ do not prevent its use, or if there are no superficial tuberculous lesions of the lung under a thin pleura; these are liable to break down under its disintegrating action.

Acute, virulent empyemata demand immediate thoracotomy,

and this is especially true after cavity rupture during pneumothorax therapy. Sauerbruch resects sections of two or three ribs and tampons the empyema cavity; but even then most of the patients die very soon. Less virulent infections that cannot be controlled by aspiration and irrigation, also demand drainage. Unfortunately any drainage stops the positive intrapleural pressure that may be indicated for the underlying pulmonary tuberculosis, which may progress rapidly, and a draining sinus may remain until death. In the hope that prolonged drainage may not be necessary, and that permanent sinus may not follow, closed, air-tight suction drainage should be tried at first if the pulmonary lesions are such as not to threaten rapid progress following expansion of the lung. Matson *et al.* report 2 complete recoveries by this method, and 3 deaths. Open drainage after resection of a few centimeters of one rib may be demanded, as for any empyema.

It is probable that a large majority of all tuberculous empyemas are complicated by bronchial fistulæ, which are largely responsible for the persistence of the empyemas. When they are small and the intrapleural fluid is not large in amount, they tend to close spontaneously and permanently; when the fluid accumulates in large amounts they may open at intervals to discharge it via the bronchial tree and mouth, and this is dangerous because of the possibility of suffocation, or aspiration tuberculosis, or pneumonia. When the fistulæ are large and do not close spontaneously, they maintain infection of the empyema and repeated aspirations and antiseptic irrigations are rarely successful; however they may be tried, and the patient so placed in bed as to favor plugging of the fistula by fibrin and cellular debris sedimented out of the fluid. Hager attempted to close them by cauterization under thoracoscopic vision. Bernou closed bronchial fistulæ in 2 cases with massive intrapleural injections of "huile gomenolée." Most cases of large bronchial fistulæ with persistent empyema fluid require eventual extrapleural or Schede thoracoplasty, which is often successful in closing them.

Results. Hedblom has recently reported a series of 74 tuberculous empyemata, all operated upon; 16 were cured, 11 in good health with sinus, 12 improved, 3 not improved, 10 operative deaths, 15 later deaths, 7 results unknown. Sauerbruch's statistics are given on page 413. In addition to their 5 cases mentioned just above, Matson *et al.* report 5 others operated elsewhere by open drainage; 3 of these died, and 2 required secondary thoracoplasty.

Postoperative Course, Complications and Management. Some surgical shock is to be expected after thoracoplasty, but it is surprising how well sick tuberculous persons withstand the major operation.

For the first few days there are pain, increased fever and pulse and difficult expectoration, and perhaps cyanosis and dyspnea. At this period, when the system is being flooded with large amounts

of toxins which have been squeezed out of the compressed lung, and a so-called negative phase exists, when general resistance is low, all tuberculous lesions are susceptible to a "flare-up." Usually within one to three weeks the symptoms of toxicity disappear, the expectoration, temperature and pulse decrease, and the appetite, weight, general appearance and mental disposition greatly improve.

There is usually considerable pain in the chest, shoulder and arm for the first days after operation, especially after the removal of the upper ribs, when the brachial plexus may be dragged upon. Sometimes the patient splints the chest by holding the arm snugly against the operated side. Persistence with active movements of the arm during the first month, as after breast amputation, almost invariably succeeds in ridding it of its stiffness and in restoration of practically perfect function. It occasionally happens that some of the intercostal nerves become entangled in scar tissue or regenerating ribs,

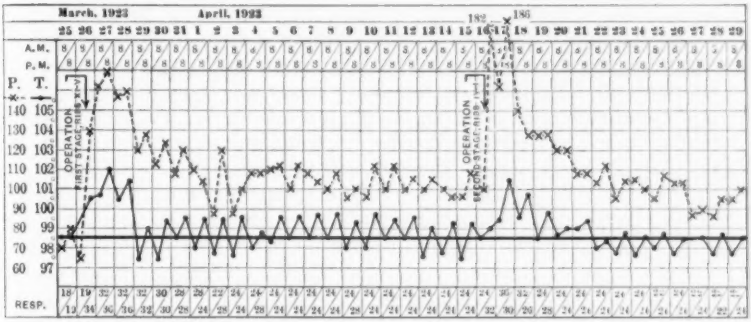

FIG. 12.—A. H., a typical postoperative chart of a satisfactory two-stage paravertebral thoracoplasty. See Figs. 3, 4, 5 and 13 for photographs of this patient.

or become caught between rib stumps, and severe intercostal neuralgia may be the result. Such cases may later need resection of the affected nerves. The posterior rib stumps may be tender to pressure, if they have been left unduly long. "Snapping scapula" may attract the patient's attention; it is due to the slipping of the vertebral border of the scapula past the posterior rib stumps.

Position in Bed. It is preferable that the patient lie slightly on the side operated upon during the first weeks after operation; this increases lung compression and rest and aids him to expectorate. Sauerbruch, with the aid of rubber rings and pillows, places the patient in the semisitting posture with the foot of the bed slightly raised, and inclines him a little toward the side operated upon by putting a pillow under the other side.

Poisoning from local anesthetic has been discussed under the section "anesthesia."

Because of the operative trauma and of the squeezing of many

toxins into the general circulation, the temperature and pulse mount rapidly after operation; 39° C. and 120 pulse are to be expected. Usually at the end of a week they decline to normal (if the operative indications and compression have been favorable). If temperature and pulse remain very high for more than a week the prognosis is poor; if they fail to drop to nearly a normal level within two to three weeks, pneumonia or a spread of the tuberculous disease is to be feared, and especially if the temperature drops for some days or weeks and then mounts. Bull has reported several cases in which the temperature was 102° to 104°, and the pulse 120 to 140 for two to three days after operation, but then behaved in the usual manner; one patient died the day after operation with a temperature of 106°, and at necropsy nothing could be found to account for death.

Cough and expectoration are made difficult by operation because of pain, lessened thoracic excursion and perhaps paradoxical respiration. In order to avoid retention of secretions and aspiration pneumonia, it is of paramount importance that the patient be enabled to expectorate. Even after lung compression the secretions are easily carried by the ciliæ to the bifurcation of the trachea, from which point they must be raised by coughing. Small, frequent, ineffectual and exhausting coughs must not be permitted. Alleviation of pain is prerequisite to effective coughing; morphin must be *regularly* given in doses sufficient to permit coughing; Sauerbruch gives them for ten to fourteen days, and then stops them altogether. During the first few days after operation it is important that a nurse be in constant attendance at the bedside to support the operated side during every coughing spell; she slips one open hand around to the back of the chest, and places the other anteriorly, and exerts gentle pressure. She urges a deep breath and a good cough. Eloesser advises turning the patient in bed twice a day in order to aid the patient to "drain out" the accumulated secretions. Simple retention of secretions may sometimes be differentiated from true pneumonia by the facts that the sputum is less rather than more in amount, and that there is no undue dyspnea or bad general condition, and that when the secretions are finally expectorated the temperature drops.

During the first few days after operation the amount of sputum is greatly increased, and then it rapidly decreases. The sputum curve, which closely follows the temperature and pulse and weight curves, is of great importance for prognosis. Between the first and second stage operations there is usually first a decrease in sputum amount, and then an increase; however, if the final stage operation is followed by a decrease and then an increase the prognosis is not good. Within a few months of many successful thoracoplasties sputum completely disappears. It is possible that the active tuberculous disease might have been completely checked, but the cavity not entirely obliterated and its walls secrete 5 to 10 cc of sputum, with or without tubercle bacilli. The tremendous improvement in

sputum, temperature, pulse and weight curves, and in the general condition of the patient are frequently so sudden as to seem a miracle. Sputum that was characterized by pus and semisolid lumps before operation becomes shiny, frothy mucus and the tubercle bacilli at first degenerate and then disappear. Disappearance of the bacilli may take several months, but their persistence does not necessarily mean that the prognosis is bad, as it is known that a few small "open" lesions may persist for many years in clinically well persons.

After every thoracoplasty there is some circulatory disturbance (Jessen), and camphor, caffein, digitalis and possibly oxygen inhalations may be indicated. Loosening or tightening of the dressings may be of service. The cardiac displacement is well withstood, and most often is simply the return of the heart and mediastinum from the position to which it had been drawn by the shrinkage of the tuberculous lung to its old normal position. The great intrathoracic vessels are never kinked or stenosed. Guilleminet has reported a partial stenosis of the subclavian vein for several days. Permanent extra load is imposed upon the heart only when the lung and its bloodvessels become greatly narrowed by the compression and new fibrous tissue.

A certain amount of dyspnea may be expected for a week; it may be caused by the toxemia, the pain, or the cardiac disturbances, if they occur, and by the paradoxical respiration and mediastinal encroachment upon the better and functioning lung. A too tight or a too loose wound dressing may be responsible. Morphin usually controls it. A high enema may remove a mass of feces and an accumulation of gas which are restricting the movements of the diaphragm. Even climbing stairs or hills months after operation may not cause dyspnea.

Wound Dressing. After operation the wound should be well protected with gauze and cotton, and firmly compressed; this is best accomplished by broad adhesive straps taking origin from the opposite shoulder and loin regions, but not from the opposite midchest, and not encircling the chest, else the function of the uncompressed lung would be interfered with and the patient distressed. Sauerbruch has 10 cm. long elastic cloth sewn in the middle of the adhesive straps in order better to aid the patient when coughing. Jacobaeus and Key make a plaster-of-Paris shield before operation to bridge the less diseased hemithorax; it rests on the hip and shoulder; after operation circular bandages may be wrapped firmly around this without prejudice to the respiration of the better lung. The wound drain used for accumulating serum, should be removed in twenty-four to forty-eight hours. The entire dressing, which soon becomes wet or stiff, and uncomfortable and a breeding place for germs, should be changed in forty-eight hours; Sauerbruch, however, does not change it until the eighth day; Ochsner and H'Doubler have sewn a wound with catgut and left a circular bandage in place for weeks, believing that it is important not to

interrupt pulmonary rest; Davies uses a many-tailed bandage and does not dress the wound for ten to fifteen days. For ease of coughing and for the patient's comfort, and in order to obtain maximum compression, it is advisable that some sort of support be worn for several months, or until the chest has become fixed by new bone formation from the rib periosteum. A convenient form of pad, taking its points of counterpressure from the opposite hip and shoulder, is pictured in Fig. 13. Leonard Freeman prefers a modified hernia truss, which touches at the spine and where the compression is desired, and leaves the uncompressed lung free for normal respiration. Bérard and Dumarest use a padded corset. Jacobaeus and Key lay sand bags on the operated side for awhile each day.

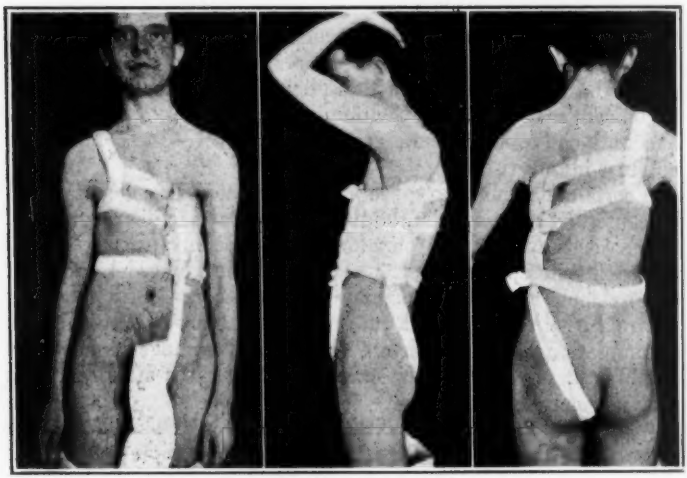

FIG. 13.—Pad and elastic band appliance worn after thoracoplasty to increase pulmonary compression.

Because of the proximity of superficial cavities and a pleura which may be latently infected, wound infection may occur more frequently than after other presumably clean surgical incisions. Burnard has reported the death of a forty-year-old man from septicemic wound infection. Stöcklin reports 8 total wound infections with 3 deaths among his 100 cases. Two of Sauerbruch's 4 cases of postoperative psychosis followed wound infection; both recovered.

Pulmonary Complications. Next to cardiac failure, spread of disease to the uninvolved portions of the compressed lung or, more frequently to the opposite lung, is the most dangerous postoperative complication. The new foci may appear as any type of tuberculous lesion, including tuberculous pneumonia, or as a non-tuberculous lobular or lobar pneumonia. The patient may become dyspneic and cyanotic, and the temperature and pulse mount rapidly; if the

disease is in the uncompressed lung, new coarse rales and the usual changes in the other physical signs may be demonstrable, but if in the compressed lung, the physical signs are so distorted as to be of no diagnostic value. In addition to the usual treatment for pneumonia, oxygen inhalations may be found useful because of the great reduction of breathing surface by the operation and pneumonic infiltration.

Postoperative hemorrhage may occur in the wound and require pressure or ligation, or a hematoma may need repeated aspirations. If there is hemoptysis from within the lung the head of the bed should be lowered and accumulation of blood, and possible aspiration prevented by insistence upon adequate expectoration.

Brauer and L. Spengler saw serous effusion appear on the unoperated side in two patients one and a half and six and a quarter years, respectively, after operation; both were acute and both were aspirated as often as dyspnea demanded, and both disappeared within five weeks.

Although miliary tuberculosis has been known to follow nephrectomy, removal of lymph glands, arthrectomy and lobectomy in tuberculous persons, it has been reported only once after thoracoplasty (Willy Meyer), and in this case a preoperative infection cannot definitely be ruled out.

The so-called "negative phase," which occurs when the system is being over- (auto-) tuberculinized by the squeezing of toxins out of the compressed lung, may be responsible for the activation of latent tuberculosis in the intestines, bones, lymph glands, epididymi or kidneys.

Sauerbruch does not permit his patients out of bed until from two to three weeks after the last operation; those who have had the two-stage operation remain under surgical supervision for about two months. Bérard and Dumarest get their patients out of bed the tenth day, and five days later return them to the sanitorium; they combat scoliosis and limitation of arm function, after the first week, with respiratory gymnastics and passive and active arm movements; their patients wear padded corsets. Stöcklin fears embolus, so he "soon" has his patients sit on a stool to exercise. Brauer also does this "soon," and places a weight on the patient's head, and has him bring one arm after the other to it; this he believes assures a straight spine and good arm function. Hug found from an examination of 22 of Sauerbruch's and Schreiber's cases that those who stayed in bed for at least six months after operation had the least spinal deformity. It is of the utmost importance that all patients who have had thoracoplasty follow a strict hygienic régime, preferably in a sanitorium, for at least six months after operation. As a result of his long experience, Sauerbruch insists that the postoperative "cure" is necessary to clinch the favorable action of pulmonary compression, as it is during the succeeding months that the fibrous encapsulation of the lesions occurs.

Physical Examination of Chest. Compression of a lung changes the physical signs of the whole chest. The uncompressed lung becomes emphysematous, and the heart and both lung outlines are difficult to determine. The heart may give forth whirrs and functional systolic murmurs because of altered conditions of position and pressure. *The compressed lung, even after its disease has become wholly arrested, presents the physical signs of active tuberculosis*, and the roentgen-ray aids but little, except that sometimes it is able to show whether or not cavities are obliterated. Judgment of the clinical condition of the compressed lung must be based wholly upon general symptoms, the temperature, weight, sputum amount, character and tubercle bacillus content, the ability to work, etc., provided, of course, that the other lung and other organs can be excluded as the sources of activity. For years the compressed lung, even in the total absence of catarrh or sputum, may be full of coarse and fine rales and a variety of bizarre noises; breathing is loud and bronchial above, and distant or absent below; the whole lung is dull to percussion, and the upper lung, because of the trachea and large bronchi, is tympanitic; fremitus may be altogether absent. Bronchiectases and cavities remaining open may give resonating rales and a Wintrich's change of note. Gross respiratory movements are minimal, except of the upper anterior chest, these being largely transmitted from the opposite side via the sternum.

The uncompressed lung shows the physical signs of emphysema which may obscure the signs of small active lesions. Attempts must be made to differentiate the rales of active disease from those transmitted from the inactive, compressed lung.

Deformity. After the old Brauer-Friedrich operation deformity and functionable disability were considerable; after the modern paravertebral operation there is rarely any appreciable deformity, certainly none that can be detected through the clothes, and no appreciable loss of arm and shoulder function. Certain anatomical changes do, however, occur, and to a more marked degree in the plastic chests of young people with weak musculature than in stout, middle-aged people whose strong muscles and ligaments make for thoracic stability. Archibald and Brauer report almost no deformity after thoracoplasty, but Hug, after a detailed examination of 22 of Sauerbruch's and Schreiber's operated patients who were found still "curing" at Davos, found some deformity in all of them, and almost all of which, in his opinion, might have been prevented by a sufficiently long postoperative rest in bed (that is, prevention of early weight bearing by the spine), and proper pad and bandage support. Stöcklin orders supporting corsets only in rare cases; Bérard uses them. Deformity does not reach its maximum for one year, unless checked by gross regeneration of bone from the remaining rib periosteum.

Hug, an orthopedist, thinks the likelihood of severe skeletal deformity after thoracoplasty upon patients less than twenty-years old

should create at least a tentative contraindication to the operation. He would attempt to obtain the desired compression with a partial pneumothorax and a pneumolysis, which are non-deforming. On the other hand Brauer and Sauerbruch would expect little deformity after thoracoplasty upon young persons if only short lengths of rib were removed.

The narrowing of the chest occurs chiefly in two directions: (1) A marked diminution in the horizontal diameter. Hug measured 3 patients at the xiphoid level and found the differences between the operated and unoperated sides to be 7, 11, and 13 cm. respectively

FIG. 14.—M. D., little gross deformity; the scars have been inked for the photograph. No functional disability. Operation one year ago. Now no expectoration nor any other evidence of active tuberculosis.

(see Fig. 2). (2) A sinking or settling of the whole hemithorax for a distance of one or two interspaces; the cut end of the peripheral first rib stump takes its place opposite the central stump of the third rib. The shoulder and axilla usually sink 1 to 5 cm., but may sometimes actually be held higher than normal by the semiconscious efforts of the patient. The vertebral border of the scapula may be caught beneath the vertebral stumps of the ribs. The clavicular fossæ are deepened, and the costal border may bulge or settle toward the iliac crest. If the lower intercostal nerves have been paralyzed the hypochondrium and epigastrium may protrude,

especially on straining and coughing. The chest just below the scapula may be much depressed. The opposite emphysematous lung causes its hemithorax to expand and to shove the lower sternum toward the operated side and to tilt it toward the compressed lung. Because of some cervical kyphosis the head may bend slightly forward, and the face turn toward the operated side; the central ends of the first and second ribs may appear as prominences in the supraclavicular triangle.

Thoracoplasty is usually followed by some scoliosis, but it is rarely of marked degree. Prior to operation the more diseased lung has usually caused a scoliosis concave toward the same side. Thoracoplasty upsets the thoracic balance, detaches muscles and ligaments, and the supporting muscles of the side operated upon atrophy to some extent; as a result the original spinal curve straightens out, and often forms in the opposite direction, that is, convex toward the operated side. The maximum convexity is in the upper two-thirds of the chest. The amount of scoliosis is roughly proportional to the number and length of ribs resected, and to the lengths of the posterior stumps, as well as to the youth of the patient and skill in post-operative management.

After months some compensatory scoliosis, in the opposite direction, appears in the cervical and lumbar spines. Because of the operative traumata to the paravertebral muscles, the scaleni and the diaphragm gain an advantage in strength over the posterior spinal muscles, and slight kyphosis results. Brauer declares that he has never seen these kyphoscoliotic changes described by Hug, but Stöcklin writes that they always occur to a slight extent.

Operative traumata to muscles, ligaments and ribs, and the subsequent scar formation combine to immobilize, or almost to immobilize, the hemithorax, and the thoracic spine becomes almost rigid, movement occurring in the cervical and lumbar regions. This functional impairment of the chest is scarcely known to the patient, subjectively, but it does serve to obtain the much desired pulmonary rest.

Results. Because the prognosis in pulmonary tuberculosis is notoriously uncertain, and because its surgical therapy is in a state of flux and imperfectly standardized, it is not entirely trustworthy to base judgment of surgical treatment upon statistical reports. The majority of patients presenting themselves at one clinic may be well-to-do and able to continue hygienic treatment after operation as long as advised to do so, and may be in the earlier stages of the disease; if they are carefully sifted for operation according to a rigid observance of predetermined indications and contraindications, and if operated upon skilfully and completely, and wisely cared for after operation, the results may well be expected to be excellent—and so they are. If another clinic accepts for operation patients with bilateral tuberculous activity, and performs incomplete and partial operations in the hope that at least a little good may be

accomplished, and does not insist upon adequate postoperative hygienic régime, disappointments are certain and the ultimate clinical results may be expected to be bad. Table II clearly demonstrates the difference between these two types of clinic.

Sauerbruch has reported 134 patients (35 per cent) cured out of his first 381 cases, which were operated upon according to a great variety of methods; there was a mortality of 2 per cent during the first days, and 10 per cent additional within the first four weeks, and 23 per cent additional after the first month, a total mortality of 35 per cent; the remaining 30 per cent included many "improved," some "no change," and a few "worse." Percentage figures for his 339 thoracoplasties, supplemented sometimes with other operations, (and which correspond closely with the figures given by other most experienced surgeons) are: cured and improved 61.6 per cent; worse and early and late deaths, 33.6 per cent; miscellaneous (no change, under treatment, and result unknown), 4.8 per cent. Stöcklin and Schreiber report 62.5 per cent "positive results," and 37.5 per cent "negative results." My collected series of 1024 cases reported during the past six years, shows: cured, 32 per cent; improved, 26 per cent; worse, and early and late deaths, 35 per cent; miscellaneous, 7 per cent. Many interesting facts may be gathered from a careful study of Tables I and II.

Mühsam and Zinn deny the permanency of the early favorable results of thoracoplasty, and say that because it is rarely able to produce sufficient compression, relapse occurs after one or two years. It is true that incomplete operations may cause an initial improvement, but are not enough to render the disease permanently quiescent. There are a considerable number of patients who are now known to have been perfectly well and able to do hard work for six or ten years and more after the complete operation, and these undeniably demonstrate the permanency of thoracoplasty results. Some patients properly operated upon do die after initial improvement, but with rare exceptions these deaths are directly due to progression of the disease in the uncompressed lung, or in other organs than the lung—disease which is beyond the control of the operation, except insofar as it is able to raise the general bodily resistance. Brauer estimates that tuberculosis progresses in the better lung after operation in 10 to 15 per cent of all cases.

The immediate operative mortality of thoracoplasty upon well selected cases is about 2 per cent. If every complication that might be attributed directly to operation is counted, and the time not limited to the first few days after operation, the mortality is from 10 to 15 per cent; 12.3 per cent is the figure for my 1024 collected cases; 10 per cent is Bull's and also Saugmann's figure; Bull reported a mortality of 11.9 per cent among 67 operations during eight years by Norwegian surgeons other than himself. Some years ago Wilms reported 23 cases, operated by himself by his technic, without an operative death.

TABLE I.*—TABULATED RESULTS OF 1024 THORACOPLASTIES REPORTED 1918–1923.

Reporter.	Year reported.	Number of patients.	Apparent complete cure.†	Clinical cure ‡	Considerable improvement.	Improvement.	No change.	Worse.	Under treatment.	Result unknown.	Deaths.	Remarks.
Archibald . . .	1923 and 1924	40	5	..	10	5	1	..	4	1	14 (1, 6 days after 2-stage Brauer-Friedrich operation, 1912; 1 heart failure, 12 days; 1 wound infect., 21 days; 2 following 3d stage op. of ant. apicolysis (pur. bronchitis, 6 days; heart failure, 15 days); 9 after 7 weeks (1 typhoid, 8 tuberculosis))	13 (5 "consid. impr.," 3 "impr.," 4 "under treat.," 1 "result unknown") have been under treatment less than 1 year; rib 1 resected in all but earliest cases; otherwise typical Sauerbruch resections; 3 had partial thoracoplasty added to partial pneumothorax; 5 had 3d-stage pneumolysis and muscle "fill;" almost all had some tuberculosis in the better lung.
Brauer and Spengler . .	1923	35	..	13	..	15	..	3	..	..	4 (1 tbc. opposite lung, 8 weeks; 1 better lung full of scar tissue (so asphyxia); 1 aspiration food to opposite lung while laughing, 10 days; 1 sputum aspiration to opposite lung, 12 days)	All by Brauer's subscapular, paravertebral op.; this partition of the 35 patients derived from calculation from author's statement that 4 died, 38 per cent "very well influenced or practically healed" and 42 per cent "substantially improved."
Brown and Eloesser . .	1923	5	..	3	2	..	..	..	..	..	.....	Observed 1 to 2 years; all women; all chronic fibroid tbc. with cavity (3, huge); in 3 slight disease by roentgen-ray (rales in 1) in better lung, but no progression occurred.
Bull	1922	75	25	..	..	..	9	..	12	..	29 (8 from operation; 20 from tbc.; 1 from other cause)	64 of the 75 observed 1 to 8 years: 38 alive, 25 clinical cures, 26 dead; 37 observed 3 years and more: 12 clinical cures, 1 has tbc., 3 uncertain, 21 dead (4 of op., 16 of tbc., 1 of flu); the 9 "no change" cases classified by reporter as "alive and tuberculous."

Burnand . . .	1922	7	..	6	..	..	..	..	..	..	1 (septicemia from wound infection)	Roux the surgeon: "Results so satisfactory, so rapidly satisfactory, so complete."
Christensen . .	1919	13	..	..	7	..	..	..	..	..	6 (of tbc., 2 to 15 months; 0 operative deaths)	6 of the 13 had bilateral disease; 10 operated at one sitting; the 7 "considerable improvement" cases classified by reporter as "more or less working."
Cordier and Gardère	1923	1	..	..	..	1	..	..	..	..	.....	Very small resections.
Descarpentries .	1923	2	..	..	2	..	..	..	..	..	.....	Resects only a few cm. anterior to and 1 to 2 cm. posterior to rib angles; never resects rib I; observed 7 and 18 mos.
Edwards . . .	1923	3	..	..	..	1	..	..	1	..	1, 3d day of heart failure	2 patients questionably suitable for op.
Frisch	1921	1	..	1	..	..	..	..	..	..	.....	Cavities and great retraction of hemithorax and traction on heart, which decompensated; all corrected by Wilms operation.
Gravesen (Saugmann) .	1923	105	..	41	2	21	..	3	..	..	38 (9 operative deaths; 29 later of tuberculosis)	Of the 21 "impr.," 2 died later of influ.; some had supplementary parasternal resections and 3 had pneumolysis (1 fat "fill" cured; 2 gauze "fill" (1 gt. impr.; 1 died later)).
Guillemenet . .	1923	27	9		5	..	1	3	5	..	4 (3 operative deaths, 3 to 12 days; 1, 3 months after op. (had bronch. fistula))	Op. by Bérard, Santy, Patel, Roux and Leriche; wide resections; of the cures, 3 were partial op.; 2 of those under treatment suffered from tbc. empyema.
Hannema . . .	1918	1	..	..	1	..	..	..	..	..	.....	Cavity and hemorrhages before ant. and post. Wilm's op.; "saved her life;" observed 15 months.
Hauke	1923	9	..	3	1	..	1	1	3	..	.....	3 to 9 months' observation.
Jacobaeus and Key	1923	44	12	..	..	8	..	3	..	..	21 (5 operative deaths, 7 days to 1 mo.; 11, later of tbc.; 5 of other causes)	These patients all operated upon over 1½ years; in 46 some pathology by ph. exam. or roentgen-ray in better lung; in 6 slight hilus thickening; only 8 absolutely negative.
Jacobaeus and Key	1923	16	3	..	..	11	..	2	..	..	.....	These patients observed less than 1½ yrs.
Jessen	1921	(20)	..	..	..	..	..	..	..	..		"10 favorable and 10 unfavorable results;" these 20 cases are insufficiently classified to be included in table totals.
Johnston . . .	1922	1	..	..	..	1	..	..	..	..	.....	1st stage, ribs I to V anteriorly; 2d stage, 3 months later, 5 to 10 cm. of ribs XI to V posteriorly.

TABLE I.*—TABULATED RESULTS OF 1024 THORACOPLASTIES REPORTED 1918–1923.—(*Continued.*)

Reporter.	Year reported.	Number of patients.	Apparent complete cure.†	Clinical cure.‡	Considerable improvement.	Improvement.	No change.	Worse.	Under treatment.	Result unknown.	Deaths.	Remarks.
Lilienthal . . .	1923	12	1	..	1	7	..	..	..	1	2 (within 4 days of op., of acute pulmonary edema)	Sauerbruch technic; always took first rib; in 1 he added pneumolysis and fat graft; in 4, preliminary resection of phrenic nerve; 3 of the 7 "improvement" had tbc. empyema.
Meyer, Willy . .	1923	5	1	..	..	1	..	..	..	..	3 (miliary tbc.; 6 days after 2d stage; 48 hours after 1st stage, probably from novocain poisoning)	All had more than a little active disease in the better lung; first rib not resected except in the "improvement" case (improvement only temporary); this patient had tbc. empyema and cold abscesses and bilateral disease; the cured patient has been well 4 years.
Moreau and Olbrechts . .	1923	1	..	..	1	..	..	..	..	..	.....	139.5 cm. resected; observed 9 months.
Mühsam . . .	1919	8	..	..	..	1	..	1	..	..	6 (1 aspiration under narcosis; 2, 1 day; 3, 17 days; 4, 2½ months of tbc.; 5, improved, but death 3 years later, Potts; 6 improved for 4 years, then died in 6 months of tbc.	All but deaths 2 and 3 presented ideal indications for operation; does not mention technic used; believes poor results due to post-war economic conditions in Germany.
Nyström . . .	1919	13	..	9	..	..	..	..	..	1	3 (tbc. some months after op.	Quoted by Madinier.
Ochsner . . .	1923	4	..	..	1	..	..	..	..	..	3 (1 op. shock, day of 1st stage, ribs X to V; 1 of tbc., 2 years postop. (had been greatly improved for 1 year); 1 of acute non-tbc. abd. illness after being cured of tbc.)	Considerably improved patient had only ribs X to VII resected; none of the others had ribs I or XI resected.
Ranzi	1922	12	..	5	..	2	..	2	..	1	2 (1 operative death, 7 days; 1 after 4 months)	Resected rib I unless clinical findings and roentgen-ray showed apex "relatively free."
Riviere and Romanis . .	1923	2	..	..	1	1	..	..	..	..	.....	Resect relatively short rib lengths.

Sauerbruch . .	1920	71	28	..	12	..	..	..	..	..	31 (2 in first few days after a 1-stage op.; 1, 9 days from aspiration; 28 died later)	These by old Brauer-Friedrich op. (9 op. in 1 stage, 38 in 2 stages, 24 in 3 stages).
Sauerbruch . .	1920	223	84	..	6	41	..	..	..	18	74 (3 operative deaths; 26 in first 3 weeks, pneumonia, aspiration, mediastinitis, progression tbc. in better lung; 45 after 4 months)	Sauerbruch paravertebral operation; 84 cures observed 1½ to 6 years.
Sauerbruch . .	1920	26	15	..	..	3	..	2	..	5	1 (pleural infection following operative tear of pleura)	
Brunner (Sauerbruch) .	1922	116	18	..	27	31	..	12	..	..	28 (13 within 4 weeks: 1 on second day, 12 after second week from heart, pneumonia and wound disturbances; 15 deaths 1 to 12 months, mostly from progression tbc. in better lung)	Partial thoracoplasty (usually ribs I to VII), combined with partial pneumothorax; cures observed 1½ to 5 years.
												Reported by Brunner; cases operated since those published in 1920; none of the 27 "considerable improvement" cases had tubercle bacilli at time of report.
Sayago and Allende	1921 and 1922	2	..	..	1	1	..	..	..	..	.....	"Improvement" case observed only 1 month; 1st rib not removed; "considerable improvement" case had basal disease and cavity, and only ribs X to VII were resected.
Schottmüller . .	1918	1	1	..	..	..	..	..	..	..	.....	Was advanced tbc.; observed 3 years.
Shivers . . .	1923	27	3	4	2	1	1	3	2	1	10 (5 during first week; 2 during first month; 1 during second month; 2 after 2 months (including 1 after 2½ years' improvement); the causes of death: pneumonia, wound infection and influenza)	1 Schede and 26 Sauerbruch operations; 1st rib resected in 3 cases; pneumolysis attempted in all but 3.
Shortle and Gekler	1922	4	..	..	2	..	..	..	..	..	2 (1 from heart failure and dropsy after first stage; 1 from heart failure ninth wk.	Both deaths occurred in patients who were "terrible risks."
Stöcklin . . .	1922	100	37	..	5	19	..	1	..	..	38 (24 early deaths: 11 heart failure, 3 wound infection, 4 aspiration pneumonia, 2 hemoptysis and aspiration pneumonia, 2 emboli, 1 novocain poisoning, 1 nephritis, 11 deaths of tbc., 3 months to 3 years; 3 deaths from intercurrent disease after improvement for 4 months to 1 year; no deaths in last 18 cases—careful selection)	All operated by Schreiber 1913–1920; extensive (110 to 140 cm.) resections of ribs XI to I inclusive, and in addition most had apicolysis without "fills;" most all were advanced tbc. with cavity and "cure" had failed; 30 had partial pneumothorax at time of op.; 25 of the 37 cured patients were observed over 2 years; 3 of the "improvement" cases relapsed after being "cured" 4 to 5 years.

TABLE I.*—TABULATED RESULTS OF 1024 THORACOPLASTIES REPORTED 1918–1923.—(*Continued.*)

Reporter.	Year reported.	Number of patients.	Apparent complete cure.†	Clinical cure.‡	Considerable improvement.	Improvement.	No change.	Worse.	Under treatment.	Result unknown.	Deaths.	Remarks.
Welles	1923	11	1	..	6	1	..	..	..	..	3 (2 after 2 weeks from wound sepsis and pneumonia in better lung; 1 after 5 months, of tbc.)	In all but 1 (later required pneumolysis and "fill"), 3 to 17 cm., ribs XI to I resected; 4 of the "consid. impr." still under sanitorium treatment.
Whittmore and Chaffin . . .	1921	1	..	..	..	1	..	..	..	..	.....	Resected 2 to 11.5 cm. ribs I to XI, inclusive, and added a small pneumolysis without "fill."
Total . . .	...	1024	243 (23.8 per cent)	85 (8.3 per cent)	95 (9.3 per cent)	173 (16.8 per cent)	13 (1.3 per cent)	36 (3.5 per cent)	27 (2.6 per cent)	28 (2.7 per cent)	324 (31.6 per cent) — 126 (12.3 per cent) were directly connected with operation; 198 (19.3 per cent) not directly connected with operation	Most of the late deaths were from tuberculosis of the originally better lung; some, however, were from intercurrent disease.

* Time intervals between operations and publication of reports vary so widely that no attempt has been made to tabulate them; occasionally they are mentioned under "Remarks."

† Classification of clinical results varies greatly according to the individual interpretation of the observer. It is widely accepted, however, that "complete cure" should be defined as freedom from any symptoms of tuberculous activity for at least one and a half years, no sputum, and ability to perform a full day's work.

‡ "Clinical cure" may be defined as freedom from any symptoms of tuberculous activity for at least one and a half years, no tubercle bacilli, but a few cubic centimeters of mucoid sputum, and ability to do a short day's work.

TABLE II.—TOTALS FROM TABLE I PARTITIONED ACCORDING TO TECHNIC EMPLOYED.

Class I*	824
Class II†	200
Total cases	1024

	Class I.	Class II.	Total cases.
Apparent complete cures	205 (c. 25%)	38 (19%)	243 (c. 24%)
Clinical cures	71 (c. 9%)	14 (7%)	85 (c. 8%)
Total cures	276 (c. 33%)	52 (26%)	328 (c. 32%)
Considerable improvements	56 (c. 7%)	39 (19.5%)	95 (c. 9%)
Improvements	159 (c. 19%)	14 (7%)	173 (c. 17%)
Total improvements	215 (c. 26%)	53 (26.5%)	268 (c. 26%)
Total cures + total improvements	491 (c. 60%)	105 (52.5%)	596 (c. 58%)
Worse	32 (c. 4%)	4 (2%)	36 (c. 4%)
Early deaths	102 (c. 12%)	24 (12%)	126 (c. 12%)
Late deaths	143 (c. 17%)	55 (27.5%)	198 (c. 19%)
Total deaths	245 (c. 30%)	79 (39.5%)	324 (c. 32%)
Total worse + deaths	277 (c. 34%)	83 (41.5%)	360 (c. 35%)
Miscellaneous (no change, under treatment and result unknown)	56 (c. 7%)	12 (6%)	68 (c. 7%)

* Patients of the 14 surgeons who were conservative in selecting for operation, and who used standard technic, resecting first rib and sufficient lengths of the others.

† Patients of the 19 surgeons who have not regularly strictly observed conservative standards in selecting cases or who have not regularly performed the complete operation.

Almost every one of the 1024 cases collected in the accompanying tables was desperate, and the disease extensive and severe before operation; almost all had cavity formation and many had bilateral, active lesions, although much worse on one side; almost all had "cured" in sanitoria under competent supervision for one, two, three, five or more years and were unimproved or worse, and in none of them was spontaneous healing to be expected; almost without exception every one was expected surely to die of tuberculosis; artificial pneumothorax had been attempted in all, and had failed because of adhesions. That any appreciable number of such desperately diseased persons could be saved from imminent death is surprising, but that 32 per cent of them actually were cured is almost miraculous. For such cases nothing is known to compare in effectiveness with compression therapy (pneumothorax or surgery), and it deserves the active, aggressive support of every physician and surgeon to whom the tuberculous come for advice.

Conclusions. 1. On account of pleural adhesions many patients with largely unilateral pulmonary tuberculosis do not obtain from artificial pneumothorax the full benefit of lung compression therapy.

2. Many among them are in sufficiently good general physical condition for surgery. The operation of choice is paravertebral thoracoplasty.

3. Any tuberculous lesions in the better lung must be inactive or only slowly progressive, if surgery is to be undertaken.

4. Cauterization, under thoracoscopic vision, of adhesions that are preventing adequate lung compression by pneumothorax should be reserved for those that are long, narrow and few in number.

5. In suitable cases operation should be performed as soon as artificial pneumothorax has proven itself ineffective; procrastination may rob these patients of an excellent chance of complete cure.

6. Thoracoplasty should be done in two stages, from two to three weeks apart. No fewer than 125 cm. of ribs XI to I inclusive should be resected.

7. Local-regional anesthesia is indicated for patients whose daily expectoration is more than 40 cc. When less than 40 cc a combination of nitrous-oxide-oxygen narcosis and local-regional anesthesia is best.

8. The immediate and remote dangers of any operation that compresses only a part of a hemithorax are greater than its advantages, except in unusual cases. This does not apply to a combination of partial thoracoplasty and partial artificial pneumothorax.

9. Neur-exæresis of the phrenic nerve may be performed with advantage before every thoracoplasty and after every artificial pneumothorax.

10. Some stiff-walled apical cavities are not obliterated by paravertebral thoracoplasty. The supplementary operation of parasternal thoracoplasty, or of pneumolysis with muscle, fat, gauze or paraffine "fill" should be considered, but not performed sooner than six months after the primary operation.

11. Some cavities cannot be collapsed, and by retention of secretions cause severe toxemia. Drainage is occasionally indicated for them.

12. Tuberculous empyema is best treated by repeated aspirations and air replacements, and sometimes with antiseptic instillations or irrigations. Only in the presence of dangerous secondary infection may open or closed tube drainage be used. Persistent empyemas, especially if complicated by fistula, often require thoracoplasty for their cure.

13. Favorable results in the surgery of pulmonary tuberculosis depend upon great discretion in the selection of cases, early and skilfully executed complete operations and strict attention to postoperative care, including not less than six months "curing," preferably at a sanitorium.

14. Among 1024 cases of advanced tuberculosis, reported from 1918 to 1923, there was a mortality of 12 per cent during the first month after operation (the immediate operative mortality was about 2 per cent), and 19 per cent thereafter, mostly from tuberculosis in the originally better lung or other organs. Twenty-six per cent were improved, and 32 per cent cured. Of the 824 patients managed according to the criteria given in paragraph 13, immediately above 26 per cent were improved, and 33 per cent cured. Of the 200 cases not so managed 26.5 per cent were improved, but only 26 per cent cured.

A complete bibliography for 1898–1923, inclusive, will appear in the author's reprints.

REVIEWS.

OBSTETRICAL NURSING. A MANUAL FOR NURSES AND STUDENTS AND PRACTITIONERS OF MEDICINE. By CHARLES SUMNER BACON, PH.B., M.D., Professor of Obstetrics in the University of Illinois, Medical Director, Chicago Lying-in Hospital, etc. Second edition. Pp. 324; 126 illustrations. Philadelphia and New York: Lea & Febiger, 1924.

THIS manual presents the theory of obstetrics combined with directions for nursing obstetric patients. It is well arranged, and the scientific side does not over balance the practical. It is simply written, the directions for all nursing procedures are clear, and should be comprehended by the practical nurse as well as by one who has had the advantage of hospital training. For this reason the manual is a good book for the obstetrician as it will better enable him to direct the work of his assistants. A few solecisms remain in the second edition, such as the reference on page 131 to sewer gases from poor plumbing as a source of infection to the parturient.

W.

VENEREAL DISEASE. By HUGH WANSEY BAYLY, M.C., Honorary Secretary, Society for the Prevention of Venereal Disease, London, Eng. Second edition. Pp. 170; 58 illustrations. New York: The Macmillan Company, 1924.

READERS will recognize the author as the leading propagandist in England for venereal disease prevention and a long preface to this book recounts the difficulties and opposition that he has met and overcome as Secretary of the Society for the Prevention of Venereal Disease. His point of view is excellently taken, his arguments are scientifically irrefutable and his fight has made the moralist and religious obstructionist recognize that "intolerable and illogical anachronism that the most easily controlled and most wide-spread and, with the exception of tuberculosis, probably the most deadly of chronic infectious diseases, should be specially selected for exemption from regulations as to prevention, notification, segregation and enforced treatment." The text is short but thorough. The outline of therapy dogmatic but safe, and it should find a place among the books of every venereal officer.

R.

MANAGEMENT OF THE SICK INFANT. By LANGLEY PORTER, B.S., M.D., M.R.C.S. (ENG.), L.R.C.P. (LOND.), Professor of Clinical Pediatrics, University of California Medical School; Visiting Physician, San Francisco Children's Hospital; Consulting Pediatrician, Babies' Hospital, Oakland; Consulting Pediatrician, St. Mary's Hospital, San Francisco; and WILLIAM E. CARTER, M.D., Assistant in Pediatrics and Chief of Out-patient Department, University of California Medical School; Attending Physician, San Francisco Hospital, San Francisco. Second edition. Pp. 659; 54 illustrations. St. Louis: C. V. Mosby Company, 1924.

THE second edition of this work remains a valuable book for the intern and general practitioner. The consideration of the more common symptoms separately, the preciseness of the therapeutic recommendations, the large number of very excellent illustrations, the glossary of formulas and recipes, and the generous list of useful prescriptions, make it a most acceptable book for the man not specially trained. The new edition contains a new chapter on Prematurity and several minor changes. The publishers have succeeded in producing a book highly pleasing to the eye of the reader. S.

L'ANGINE DE POITRINE. By PROF. DANIELOPOLU, Director La Deuxieme clinique medical de l'Université de Bucarest. Pp. 113; 31 illustrations. Imprimerie Cultura, Bucarest, 1924.

THIS 113 page monograph covers the pathogenesis of angina pectoris from the point of view of physiology and pathology. The hypotheses concerning the cause of anginal pain are enumerated and the treatment of this disease is discussed briefly from its medical aspects and fully from the surgical side. An extensive bibliography is given and to one interested in this special topic the monograph is valuable. P.

DISEASES OF THE NOSE, THROAT AND EAR FOR PRACTITIONERS AND STUDENTS. Edited by A. LOGAN TURNER, M.D., F.R.C.S., Senior Lecturer on Diseases of the Ear, Nose and Throat, University of Edinburgh. Pp. 413; 222 illustrations and 12 plates, 8 in color. New York: William Wood & Co., 1924.

THIS present work, written by those engaged in the teaching and practice of the specialty in the Edinburgh Medical School, is in reality a revised and rewritten fourth edition of the text-book by the late W. G. Porter, who was killed in battle in 1917. It is

remarkably thorough, concise and complete for a volume of this size and can be studied with profit even by those far advanced in special work. It is entirely up to date, the illustrations being especially noteworthy for their clearness and their originality. The entire book is well written and printed, and in such a concise manner that practically every subject is adequately treated, even to a description of the anatomy of the parts under consideration. C.

THE INTERNAL SECRETIONS. By ARTHUR WEIL, M.D., Assistant Professor of Physiology at the University of Halle. Authorized translation of the third German edition by JACOB GUTMAN, M.D., PHAR.D., F.A.C.P., Director, Brooklyn Diagnostic Institute. Pp. 287; 45 illustrations. New York: The Macmillan Company, 1924.

INSTEAD of chapter headings entitled "thyroid," "pituitary," "adrenals," etc., which one is accustomed to expect in works upon this subject, one finds in this book chapters upon the blood, circulation, respiration, metabolism, growth, reproduction, etc. This original angle of presentation possesses certain advantages, in addition to which the excellence of the translation, the brevity of the work and its accuracy of statement render it of interest and value to the physician and student alike. A.

FERTILITY AND STERILITY IN HUMAN MARRIAGES. By EDWARD REYNOLDS, M.D., and DONALD MACOMBER, M.D. With a section on the Determining Causes of Male Sterility. By EDWARD L. YOUNG, JR., M.D. Pp. 275; 17 illustrations. Philadelphia and London: W. B. Saunders Company, 1924.

THE chapter on the clinical conduct of a case of sterility is the keynote of the book. It describes with such thoroughness and detail the methods to be used in dealing with the crux of this puzzling medical problem, the diagnosis of the cause, that it may be well singled out for mention in a very readable and well-balanced book.

There is a clear statement of the general biological and physiological problems in the subject as a whole. All the determining causes in the female are taken up in succession. Dr. Young has contributed an excellent section bearing on the aspects of sterility and infertility from faults in the male.

Relative infertility, repeated interruptions of pregnancy, one-

child sterility, the marital habit and the prophylaxis of sterility from pubertal and menstrual hygiene are discussed. Animal experimentation in regard to diet—calcium values and abstraction of vitamins—is referred to with what bearing it may have in the human. Endocrinology is dismissed with a wave of the hand. The final chapter on the surgery of sterility describes various gynoplastic procedures, and gives the authors' conclusions regarding transuterine insufflation of the tubes. W.

HUMAN PHYSIOLOGY: A PRACTICAL COURSE. By C. G. DOUGLAS, C.M.G., M.C., D.M., F.R.S., Fellow of St. John's College, Oxford, and J. G. PRIESTLEY, M.C., D.M., Christopher Welch Lecturer in Clinical Physiology, University of Oxford. Pp. 232; 30 illustrations. New York: Oxford University Press, American Branch, 1924.

THIS is a compilation of experiments which may be performed upon the human subject. Although designed primarily to elucidate physiological principles, the methods used find an application in applied physiology. The laboratory directions are interpolated with the theoretical basis for a proper interpretation of the results obtained.

The course covers the following subjects: Respiration, total energy exchange and energy production, the formed elements of the blood, blood chemistry, blood gases, the polygraph, blood-pressure and the functional activity of the kidneys and the alimentary canal.

The experience of the teachers of physiology during the past ten years has amply demonstrated the value of such a course, which has been advocated for many years in this country by Dr. Yandell Henderson. In addition to its practical value to the medical student, human physiology arouses a keen interest in the student with the result that he retains a more lasting impression of the fundamental physiological principles involved. The possibilities are by no means exhausted in these pages. However, the subjects treated indicate the trend which such a laboratory course may take.

In American laboratories other types of apparatus and chemical methods than those described are in use. Examples which may be cited are the substitution of the Henderson-Haldane apparatus for the original Haldane gas analyzer; the improved Van Slyke methods of blood gas analysis and the Folin-Wu sugar method.

It would seem desirable, wherever possible, in a course which forms the beginning of clinical physiology, to employ methods which the student may have occasion to use in the clinic. G.

DISEASES OF THE EYE. By DR. GEORGE E. DE SCHWEINITZ, Professor of Ophthalmology in the University of Pennsylvania; Ophthalmic Surgeon to the University Hospital; Consulting Ophthalmic Surgeon to the Philadelphia General Hospital. Tenth edition. Pp. 865, 434 illustrations, 7 colored plates. Philadelphia: W. B. Saunders & Co., 1924.

DR. DE SCHWEINITZ has brought his new edition fully up to date in every respect, and it should be in the library of not only every ophthalmologist, but every active practitioner of medicine.

The arrangement and classification of contents makes them easily accessible. The revision has been thorough, so that as a book of reference it is unexcelled, though its real value lies in the interesting detail allotted to every subject of importance.

Among new topics included for the first time are the diaphragm lamp (Gulstrand), contact illumination, binocular visual acuteness, sunlight as a source of illumination in ophthalmoscopy, ophthalmoscopy with red free light, agricultural conjunctivitis, Barraquer's method of suction extraction of cataract, and O'Conner's "Cinch" shortening operation for strabismus. S.

ESSAYS ON THE EVOLUTION OF MAN. By G. ELLIOT SMITH, M.A., M.D., LITT.D., D.SC., F.R.C.P., F.R.S. Pp. 158; 19 illustrations. New York: Oxford University Press, 1924.

THOSE of our readers who were fortunate enough to hear Professor Elliot Smith on his lecture tour in the United States last spring will need but little introduction to this book. Representing three addresses made to the British Association, the British Academy and the Royal Institution during the past eight years, it contains substantially an elaboration of the matter given in his American lectures.

In the first chapter, "The Evolution of Man," man's pedigree from the remote shrew-like mammal of the cretaceous period is presented together with a discussion of "the factors that were responsible for the emergence of the distinctive characters of man." Professor Smith's view is that the first important step was the adoption of arboreal life with the consequent enormous development of the visual cortex at the expense of the olfactory parts of the brain. With the greater need for precise movements and use of the other senses, this not only developed the motor area but evolved the great prefrontal area "concerned with attention and the general orderly coördination of psychic processes." The assumption of the erect attitude and acquisition of the power of speech are considered

enormously important incidental manifestations of the brain development, which permitted sufficient cortical regulation of skilled movements.

In the second chapter is an interesting description of the various types of primitive man (the Java ape-man, the Piltdown dawn-man, the Heidelberg, Neanderthal and Rhodesian men, and the earliest known varieties of Homo sapiens). In the dawn of civilization, the invention of agriculture, and the domestication of the dog and other animals are discussed. The third chapter, the Human Brain, deals in greater detail with the development of the theory already given.

K.

NOTES ON THE MEDICAL TREATMENT OF DISEASE FOR STUDENTS AND YOUNG PRACTITIONERS OF MEDICINE. By ROBERT DAWSON RUDOLF, C.B.E., M.D. (EDIN.), F.R.C.P., Professor of Therapeutics in the University of Toronto; Clinician, Toronto General Hospital; Consulting Physician, Victoria Hospital for Sick Children, Toronto; Fellow of the Royal Society of Medicine; Member of the Association of American Physicians; Ex-Vice-President of the American Therapeutic Society, Colonel, Canadian Army Medical Corps (Reserve), and late Consulting Physician to the Canadian Forces overseas. Second edition. Pp. 486; 4 illustrations. Toronto: University of Toronto Press, 1923.

THIS modest title does not do full justice to the practical excellence of this little textbook of medical treatment, which is full of sound medical philosophy, well written, up to date, and, for the subjects considered, is quite comprehensive. The introduction is a delightful résumé of the history of the science and art of healing. There are 29 additional chapters setting forth in concise form and with a well balanced point of view the modern methods of treating most of the important diseases met with in general practice. The book merits a larger audience than that indicated in the title. F-H.

DOMICILIARY TREATMENT OF PULMONARY TUBERCULOSIS. By F. RUFENACHT WALTERS, M.D., B.S., M.R.C.P. (LOND.), F.R.C.S. (ENG.), Medical Director, Crooksbury Sanitorium. Second edition. Pp. 288. New York: William Wood & Co., 1924.

THIS book is designed to assist the practitioner as well as the specialist in treating tuberculosis. The addition of two new chapters, one of an introductory nature, and the other on the general topic of home treatment in its public and social aspects, constitute a distinct improvement over the first edition. A.

SURGICAL PATHOLOGY. By JOSEPH MCFARLAND, M.D., Sc.D., Professor of Pathology in the Medical Department of the University of Pennsylvania. Pp. 701; 435 illustrations. Philadelphia: P. Blakiston's Son & Co., 1924.

DR. MCFARLAND has written a really valuable book—with MacCallum's Pathology and Ewing's Neoplastic Diseases it should immediately take rank as one of the three leading books on Pathology that have been written in English in the past fifteen years. In the preface, he states that the book has been written for those beginning to specialize in Surgery, who "frequently find themselves confronted by problems difficult to solve by recourse to the ordinary sources of information." Valuable as it undoubtedly will be for this class, it will be even more useful—nay, necessary—for their laboratory coöperators, who must give information, diagnosis and prognosis on the surgical tissues brought to them. Particularly satisfactory is the emphasis placed on the normal variations from typical structure, stumbling blocks which not infrequently precipitate the microscopist into the mire of pathological error.

The book is divided into three parts: (1) Congenital Conditions of Surgical Interest (204 pages); (2) Tumors (174 pages) and (3) Special Pathology (269 pages), the bibliography and index taking up the remaining 54 pages. Although the author considers that in this way "the matter has been arranged in logical order and sequence," it introduces certain disadvantages. Thus cholesteatoma, mixed tumors, dermoid cysts, mammary and fetal thyroid adenoma and hypernephroma, having been given under Part I (35 pages), are obviously missing from Part II on Tumors. Also tumors having been considered in Part II, must again be taken up under each organ discussed in Part III, a fault which is of course shared with the textbooks of general and special pathology.

The author states in the preface that he has given particularly full consideration to two kinds of subjects—"those that experience has been shown to be necessary to the student and those concerning which the author has special knowledge." Bearing this in mind, however, the reviewer feels a disproportionate space has been allotted to the congenital (first) part and that various numerous important subjects especially in Part III have been passed without any or with insufficient recognition. For instance, inflammation and infection are nowheres treated systematically, the only abscess indexed being perinephritic abscess. In special pathology, the skin, muscular and circulatory systems are conspicuous by their absence, so that aneurysms, gangrene, ulcers (except of the stomach) and similar important surgical conditions are hunted for in vain. A consistent system governing the inclusion and arrangement of various conditions is manifestly lacking—perhaps purposely so; for instance Myositis Ossificans is listed twice in the index, occurring once in a discussion of metaplasia and once as an "osteomatoid."

As one would expect, the mammary gland is treated fully and ably, as is also a five page discussion of the appendix, but that is no reason why actinomycosis should be mentioned only in these two places. The very fulness of the index offers an easy opportunity for the hasty critic to find such flaws, and yet the system of cross indexing could have been pushed even further to advantage. The spleen is only mentioned for its anomalies (another example of the over emphasis of embryonic defects), while Banti's and Gaucher's diseases and other splenomegalies are completely ignored. While this review was being written, a suspicious tuberculosis of the stomach was submitted for diagnosis. Turning hopefully to the stomach section, the reviewer found no mention of tuberculosis, syphilis or other conditions with which ulcer and cancer could be confused. Starting at the beginning of the index, the reviewer then noted the neglect of abscess, aneurysm, ascites, bedsores, boils, brain lesions, buboes, burns and then desisted.

A few suggestions might be made to the proofreader for the next edition, which will doubtless soon be forthcoming: "Pearlgeschwulst" is an unpleasant hybrid (page 73); "Endodemal" at the bottom of page 72 and "Peal" (page 76) each lack an "r"; Kirmisson, whose name occurs 16 times in the bibliography has acquired an "e" in the text (page 49); likewise Fibiger, the producer of gastric carcinoma in the rat (page 218); "Cordoma" (page 175) lacks an "h;" the word "aegagrophilus" (hair ball), if it must be used at all, should always be spelt the same way (page 577 and Index); in the index "Tumors" should come after "Tubular" and "Tuberculosis" and not before; and in the table of contents, the subheadings had better be numbered, if they cannot be properly aligned. These corrections, found in a cursory examination are only samples of many more that indicate the need for a thorough typographical revision.

The illustrations are instructive and interesting and nearly always bring out the desired point. This is more than sufficient excuse for the fact that more than three-quarters are taken from other writers. Of the remaining quarter, many already have been published by the author, a justifiable economy in these days of costly printing. A similar economy in the arrangement of the bibliography, more on the lines of Aschoff, Ewing or Kaufmann, would have either saved considerable space or permitted many more than 700 to be included in the same space. There is also a regrettable lack of completeness in the references given.

It should not be understood from these criticisms, some unavoidable and others unimportant, that the book is not considered a good one. On the contrary, it is a very welcome and valuable addition to pathological literature, and in some respects (as for instance, the clear cut presentation of the first hand views of an expert on the subject), should serve as a model for medical textbook writers. It is on account of its obvious value, that we modestly offer suggestions to make the second edition even better than the first. K.

PROGRESS
OF
MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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The After-effects of the Late Toxemias of Pregnancy.—HARRIS (*Bull. Johns Hopkins Hospital*, 1924, **35**, 103) made a study of 177 obstetrical patients in the Hospital from February 1, 1919, to February 1, 1923. There were 218 deliveries in the series, and 163 of the mothers returned for further study one year after delivery. The main point of value derived from the study lay in facts gained regarding the relation of preëclamptic and eclamptic states to renal disease. Chronic nephritis was found to follow preëclamptic toxmia in a surprisingly large percentage of cases (60 per cent). No way was found, however, to differentiate between the toxemic case that would develop renal disease and those that would not, since the behavior of the blood-pressure following delivery gave no indication. Still if sign and symptoms of toxemia persisted longer than three weeks after delivery, renal disease was always one year later. In fact, with this duration of the toxemia, the presumption is that this underlying disease is renal in origin.

Effect of Tonsillectomy on the General Health of Twelve Hundred Children.—The benefits to children of tonsillectomy become less striking when no selection of cases is made, and when the series is controlled by the same number of similar children with tonsils left intact. KAISER (*Jour. Am. Med. Assn.*, 1924, **83**, 33) brings out certain beneficial effects of the operation, however, based on a three-year follow-up study of the control series. Considerable relief is obtained from sore throat, colds, and mouth breathing. The chances for discharging ears and their complication are lessened. The incidence of diphtheria and heart disease was diminished. Malnutrition was definitely reduced following the operation. Chorea or rheumatism, measles and scarlet

fever were equally prevalent in the operated and non-operated series, although the latter two diseases tended to be less severe in the operated cases. No influence was seen on infections of the larynx, bronchi or lungs.

The Vital Capacity of the Lungs and Its Significance in Hyperthyroidism.—McNeal (*Arch. Int. Med.*, 1924, **34**, 168) has investigated the vital capacity of the lungs in cases of hyperthyroidism. He concludes from his study of a large number of thyroid cases that as a result of the marked reduction of the vital capacity of the lungs, below 70 per cent in a great majority of the severe cases of hyperthyroidism, that this reduced vital capacity points more definitely to a bad prognosis than does the degree of increase in the basal metabolism.

An Insulin-like Material in Various Tissues of the Normal and Diabetic Animal.—Since the discovery of insulin and the extensive researches that resulted have shown that insulin is ubiquitous in nature and is found in all living substances. Additional confirmation of this has been brought forth by Best, Smith and Scott (*Am. Jour. Physiol.*, 1924, **68**, 161) who found that insulin may be extracted from a number of tissues besides the pancreas, although in the pancreas the amount of insulin per unit of weight is much higher in concentration than in other tissues, but in tissues with considerable bulk as liver and blood the total amount is very much greater than the very much smaller organ, the pancreas. These findings together with the findings of insulin-like substances in plants lead the authors to the conclusion that "insulin may prove to be a constituent of every cell in which carbohydrate is metabolized and the islands of Langerhans to be specially developed structures which supply the active material when the demand for it is too great to be provided for by the insulin-producing power of the individual cell."

The Clinical Value of the Serum Tetrachlorphthalein Test for Liver Function.—There is apparently an accumulative mass of evidence which tends to show that the tetrachlorphthalein test for liver function is a valuable procedure, which is not true of practically all the other tests which have heretofore been employed, as they have not proved worthy either because of difficulty of technic in their employment or from the fact that other substances which have been injected into the body as a test of liver function were of no value because they were absorbed from the intestine or excreted by the kidney, making the tests indefinite and inconclusive. In a recent article Ottenberg, Rosefeld and Goldsmith (*Arch. Int. Med.*, 1924, **34**, 206) have brought together additional evidence to show that the test is of value in certain types of liver disease. The authors use a somewhat larger dose of the drug than it is customary to use but otherwise follow the technic of Rosenthal throughout. They feel from their study of over 100 cases that the test is useful in detecting cirrhoses, metastatic carcinoma, and cardiac decompensation and that its greatest value will probably be in the early diagnosis of these first two conditions. The test is valueless in cases of obstructive jaundice.

Effects of Intramuscular Injection of Sodium Citrate upon Bleeding.—Higgins and Fisher (*Ann. Surg.*, 1924, **80**, 268), following the experience of Neuhof and Hirschfeld with sodium citrate intramuscularly administered, studied its action on a series of 50 cases of various kinds. They found the maximum effect of the injected salt to occur in about forty-five minutes, and the clotting-time to return completely to normal in one to two days. They report lowering of the clotting-time to about one-sixth its former value, regardless of whether it was previously normal or prolonged. Since the action of the sodium citrate is supposed to be on the blood platelets, causing their disintegration, they advise against its use in cases of purpura hemorrhagica and hemophilia. It has been noticed that, following the transient shortening of the clotting-time in a hemophiliac, there occurred a considerable prolongation beyond that present before the salt injection. Thirty cubic centimeters of a 30 per cent solution of the salt is used, the injection being deep into the buttocks. Novocain injection should precede the citrate solution, otherwise the concentrated salt causes much pain and irritation.

SURGERY

UNDER THE CHARGE OF

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Actinomycosis.—Keynes, (*St. Bartholomew's Hospital Reports*, 1924, **72**, 71) says that the organism of actinomycosis is a slow, insidious and relentless enemy, whose ravages are often well advanced before its presence is diagnosed. It is certain that purely surgical measures are of first importance and should never be omitted. The seriousness of the disease demands also that every other remedy, which may be supposed to be of value, should be used at the same time. Potassium iodid, which enjoys a reputation founded on long established custom rather than on real success, should be given by mouth in huge doses. Copper sulphate solution should be injected with the lesion. Sinuses should be irrigated with the same solution. Autogenous vaccines should be given as soon as the organism is isolated. Roentgen-rays should be given in deeper lesions, radium to the superficial.

Compression Leverage Fractures of the Ankle Joint.—Stevens, (*Am. Jour. Surg.*, 1924, **38**, 134) says that these leverage fractures of the ankle under compression are all of the same etiology and vary simply from distribution of force and intensity of stress. This applies to most of the so-called simple fractures of the lower end of the fibula, since the salient features of this fracture are present, *i. e.*, ligamentous and tendon

injury and a destroyed mortise, permitting dislocation. Fractures of the inversion type are not usually attended with so great a destruction of ligaments, but there is an equal or more serious involvement of tendon sheaths and a greater posterior dislocation is common. The author feels that the majority of these ankle fractures are not tremendously serious injuries and do not deserve the bad repute, which is theirs at present. Motion, active and passive, from the very beginning is the solution of the problem. No masseur is competent to remedy any bad result, while in the hands of a man who understands the pathology of the lesion there is no danger.

Appendectomies at the Lankenau Hospital.—DEAVER and MAGOUN (*Ann. Surg.*, 1924, **79**, 854) say that acute appendicitis is, in the majority of instances, a disease of early adult life, although it may occur at any age. The mortality in this disease has decreased practically 50 per cent during the last decade and while the general increase in knowledge concerning it may partially account for this, it would seem as if the expectant treatment of spreading peritonitis is also of value. After the peritonitis has localized and a mass is present, the incision as described will be of value in the extraperitoneal approach to the ileum. In practically every case the appendix is removed, drainage varies with the situation of the abscess. Cigarette drains and pieces of gauze are commonly used, and occasionally as in pelvic abscess a glass tube is used. The highest mortality follows subdiaphragmatic abscess or multiple abscess. If the cecum or ileum is indurated or ulcerated at the primary operation, fecal fistula will occasionally occur. When the appendix with the abscess lies under the terminal ileum, obstruction may follow.

Two Hundred and Sixty-two Consecutive Cases of Appendicitis.—GOTCH and DURMAN (*Ann. Surg.*, 1924, **79**, 862) say that appendicitis is probably the most important and frequent surgical disease. About 14,000 people die annually from it in the United States. The death-rate for the present series was 7.2 per cent, while 205 cases complicated by abscess had a death-rate of 9.2 per cent. The preoperative intravenous injection of normal saline solution is advocated as a treatment for all very sick patients. The advantages of the McBurney incision are pointed out. The expectant treatment of appendicitis is not advised. The postoperative treatment consisted of the administration of plenty of fluid, by the intravenous route, if water could not be taken by mouth; sufficient morphin; starvation until peritonitis had completely subsided; and frequent examination for secondary abscesses and prompt drainage of the same.

Early Gall-bladder Pathology.—DEAVER and RIESMAN (*Therap. Gaz.*, 1924, **48**, 381) say that they have noted the strong resemblance between the symptoms of lesions in the gall-bladder and the symptoms of what later proved to be chronic appendicitis. On the other hand the senior author has had the experience of finding that appendectomy may fail to relieve a patient of his digestive troubles and on reopening the abdomen, the actual site of disease is found to be the gall-bladder. This error in diagnosis is entirely pardonable, because the differentiation in

an appendix, particularly when it is in a high position and cholecystitis cannot always be made clinically, and in addition, even with a good exposure in an opened abdomen, the presence of cholecystitis may be doubtful. Cholecystic adhesions do not always indicate a diseased gall-bladder, but they arouse that suspicion. Next to disease of the gall-bladder the most common upper abdominal disorder is duodenal ulcer, which in the senior author's experience rarely has given rise to adhesions. Therefore the presence of cholecystic adhesions may be taken to indicate not duodenal ulcer, but cholecystitis or possibly appendicitis.

Hepatitis—A Condition Associated with Gall-bladder Disease.—HEYD (*Surg., Gynec. and Obstet.*, 1924, **39**, 40) says that hepatitis in some degree is almost invariably associated with chronic disease of the gall-bladder and biliary ducts. Hepatitis may exist as the primary or secondary lesion. When hepatitis is the primary lesion, infection takes place through the portal system with secondary infection of the gall-bladder, by way of the lymphatics. When hepatitis is the secondary lesion, infection takes place from the gall-bladder by way of the extra-hepatic and intrahepatic lymphatics. In the majority of cases, the hepatitis is probably symptomless; it may occasionally be sufficiently widespread to initiate changes leading on the one hand to types of biliary cirrhosis, and on the other hand to types of portal cirrhosis. Cholecystitis may be secondary and of minor importance to changes in the liver. Some cases after operation show a marked degree of hepatic insufficiency. The liver, pancreas, gall-bladder and gastroduodenal segment, must be viewed as one physiological and pathological system, disease of one organ expressing itself in varying degrees of pathological change in the other members of the group. Pancreatitis is a frequent concomitant in either hepatitis or biliary system infection. In hepatic insufficiency or hepatic dysfunction, we find marked variations in blood chemistry.

THERAPEUTICS

UNDER THE CHARGE OF

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Further Experiences with the Insulin Treatment of Diabetes.—Having used insulin for about one year in their private clinic VON NOORDEN and ISAACS (*Klin. Wchnschr.*, 1924, **17**, 720) report that during the last half year the daily number of insulin injections has increased to about 2000 units a day. Since using insulin they have not lost a case from diabetic coma, and consider that the most striking results are obtained in the cases of precoma and coma. The prognosis of coma cases which were formerly treated with strict starvation and large doses of alcohol has been increased 50 per cent. Their most severe case of coma

required 100 units in twenty-four hours. Usually 30 units given at three-hour intervals are sufficient in these cases. Careful observation of the patient for symptoms of hypoglycemia, and observance of the blood-sugar curve should be made, and a dextrose infusion at hand to be given if necessary. In small diabetic children periods of marked acetonuria may appear between the periods of freedom from glycosuria and acetonuria. These are due to acute nutritional disturbances similar to the cases of acidosis with vomiting seen in children, and can be controlled with small doses of insulin. The smallest dose of insulin which will give the desired results should always be used. Eighty to 100 units a day may be necessary for a time, but usually 40 to 60 units is sufficient. Their routine insulin and diet treatment is: 1. Two test days when the patient receives 1 to 1½ gm. of protein per kilogram of body weight, and 100 gm. of bread; then, (2) a bed and fast day; then, (3) a bed and egg day when five eggs and 300 to 400 gm. of green vegetables or salad, and 80 gm. of fat are allowed. (Usually the urine is sugar-free or nearly so by this time.) 4. A strict diet with small doses of insulin night and morning is then begun, and the diet is gradually increased with the addition of carbohydrates, fat, and protein depending on the amount of insulin required and the condition of the patient. 5. Every five or seven days either a fast, egg, or vegetable day is required; when the morning dose of insulin only is given. 6. This test diet is not concluded unless the patient has reached a diet which he can continue at home. At least 80 to 100 gm. of bread, or its equivalent, and about 1 to 2 gm. of protein per kilogram of body weight. After two to three weeks of insulin treatment the intolerance to albumen has become much less than that to carbohydrate so that the test diet may include five to six days of diet rich in protein and fat and poor in carbohydrate. In this way the amount of insulin may be reduced. This increased tolerance for albumen is a great advance in the management of diabetics, for years of observation have shown that a protein-poor diet is desirable in reducing a glycosuria, but bad for the patient. When the patient has gained in weight and strength, and is sugar-free and acetone-free he may continue at home. *a*. Continuation of the diet on discharge with not more than two insulin injections a day. *b*. In order not to let him become habituated to the insulin a carbohydrate-free day every week is given, with only one small insulin injection in the morning. *c*. Usually each week a fast, vegetable, or egg day is ordered and the next morning the blood sugar may be so low that the insulin can be omitted. Fast days are not often ordered, and egg days are better than green vegetable days. Periods when the patient may be refractory to insulin treatment must be recognized. In these cases insulin should be tried again after a week's interval. Whether the so-called "severe cases" seen in children, young adults and sometimes in later years will be as greatly benfited by insulin as some American physicians believe, is still undecided. The moderately severe cases are the most successfully treated, and because of insulin more liberal diets can be given, the patient has more strength, energy, and feeling of well-being, and the future for him is more assured. They believe that a 25 per cent advance has been made in the treatment of this type of case over the former dietetic treatment alone, although with the insulin treatment the diet must be more strictly followed than before.

The Basis of Allergic Phenomena.—Hanzlik (*Jour. Am. Med. Assn.*, 1924, **82**, 2001) divided allergic phenomena into two classes: (1) The anaphylactic, and (2) the anaphylactoid. The former require a native or complex protein for their production as well as a period of incubation; while the latter can be produced by a great variety of agents unrelated physically or chemically, and no period of incubation is required. The symptoms of both are nearly identical although protein anaphylactic phenomena are characterized by a hyperexcitability of smooth muscle, and both phenomena appear to rest on a common basis, namely, on disturbances in the physical and colloidal mechanisms of the blood and tissues. The result of these changes is the alteration of physical functions ordinarily recognized as "reactions." That there is a mutual relationship between these reactions and pharmacological phenomena is evident and of broad significance in biology. Numerous pharmacological analogies can be given to show how drug action varies with the functional state of the organ or organism, and how a drug may have its ordinary action inhibited or reversed by previous alteration of ionic equilibrium. In the treatment of disease empirical use has been made of a great variety of substances which produce anaphylactoid phenomena. Usually diseases of unknown etiology are so treated, and the beneficial results often obtained probably depend upon the alteration in cellular function with increased capillary permeability which would aid in the removal of edema and chronic inflammations, and facilitate exchange of metabolites, increase the metabolism, etc. On the other hand the results may be alarming and even result fatally. There is no justification for the intravenous use of such agents as hexamethylene, iodid and salicylate because their ordinary systemic effects are readily and promptly obtained from oral administration, and their intravenous administration is followed by definite chemical and physical changes which indicate that they are disturbing and injurious to important functions and tissues. An agent injected intravenously may be temporarily beneficial to one function, but detrimental to others and to the organism as a whole, and the intravenous effect can not be predicted from the physical or chemical properties or from their pharmacological effects when given by mouth.

The Thyroid Treatment of the Nephroses.—Though Campanacci (*Wien. med. Wchnschr.*, 1924, **11**, 257) assumes that the action of thyroid extract on general metabolism is well known he reviews briefly the facts which various workers have discovered regarding its diuretic action, and outlines the beneficial results which he obtained by the administration of thyroid extract to 3 cases of nephrosis. Following the researches of Eppinger who first emphasized the relationship between the thyroid gland, diuresis, edema, and kidney function and showed that thyroid extract played an important part in the mobilization of salt and tissue protein it was recognized that the kidney alone was not the only important factor in the question of diuresis but that the tissue spaces of the entire body played an equally important part. Eppinger considers thyroid extract to be a diuretic with an extrarenal action, and an ideal agent in those cases where the usual diuretics cause too severe irritation of the kidney. He particularly recommends its use in cases of myocarditis and in cases of nephrosis, and recognizes

a complementary action when used in conjunction with digitalis. Eppinger advises a beginning dose of 0.3 gm. of the desiccated thyroid extract gradually increasing to 1.2 to 1.8 gm. a day. If no results are seen at the end of two weeks' administration it can be discarded as useless.

Regarding the Cause and Treatment of the So-called "Mucous Colitis."—WENT (*Deutsch. med. Wchnschr.*, 1924, **20**, 632) outlines the successful vaccine treatment of 9 cases of mucous colitis. He believes that the intestinal tract of these cases has lost its inherent protective mechanism against bacterial invasion and their products, and that the resultant inflammation causes the symptom-complex known as mucous colitis. After examination of the fecal flora of his cases he does not believe that the streptococci play an important part in the etiology of mucous colitis, but does believe that the colon bacillus through a lowered resistance of the intestinal wall becomes an important factor. He prepares vaccines from the patient's stool by growth on endo-agar for twenty-four hours, then transplants are made to plain agar slants which are grown for twenty-four hours and suspension of the growth is made in 15 cc of saline solution. Growth is killed by heating at 56 degrees, and 0.5 per cent carbolic acid is added as a preservative. One-half cubic centimeter is injected subcutaneously, and two days later 1 cc and then two days later 2 cc.

The Raw Fruit Cure.—MENDEL (*Klin. Wchnschr.*, 1924, **15**, 624) considers that the successful handling of severe disturbances of circulation with the Karell milk diet depends on the diminution of the fluid intake and the low sodium chlorid content of milk rather than on its diuretic action or the absence of irritating substances. In cases of edema due to cardiac or renal insufficiency as also in many other diseases such as acute nephritis, gout, acute eczema, etc., he advocates a diet of raw fruit in place of a Karell diet. Not only is raw fruit more acceptable to most patients, but excellent results were obtained as the sodium chlorid content of fruit is negligible, and the albumen content only 0.3 per cent. In most cases 1 kilogram of raw fruit a day is enough to satisfy hunger and thirst, and rest in bed during this diet as with the Karell diet is necessary.

PEDIATRICS

UNDER THE CHARGE OF

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Thymus of New-born, and Its Significance to the Obstetrician.—PETERSON and MILLER (*Jour. Am. Med. Assn.*, 1924, **83**, 234) observed that abnormally enlarged thymus is common in the new-born, occurring in from 40 to 50 per cent of such infants. In general few symptoms indi-

cative of thymic hyperplasia are apparent the first day of life. When these do occur they are usually mild. A tendency to higher rate of thymic hyperplasia is noted in infants born of elderly mothers and of multiparas, in male infants and in infants born at term. No appreciable difference in size or weight exists between infants showing thymic hyperplasia and those with negative thymus. There is a definite fluctuation in the size of the thymus synchronous with respiration. From a diagnostic standpoint the roentgen-ray is superior to clinical methods in arriving at an estimation of the size of the thymus. While it may be impracticable outside of a hospital to subject every new-born infant to the roentgen-ray, it is absolutely essential that every baby with thymic symptoms be so treated. Stereoscopic films of the chest taken at the end of expiration are of more practical value than fluoroscopic observations. Potential dangers from hyperplasia of the thymus may be eliminated by early diagnosis and by roentgen-ray treatment. This treatment is fairly well standardized. At a focal distance of 12 inches with a three-millimeter aluminum filter interposed the exposure is made for two to three minutes. This is less than one-half an erythemic dose. Three treatments of this character are given at intervals of one week.

Exsanguination-transfusion in Treatment of Severe Toxemia.—Robertson (*Arch. Surg.*, 1924, **9**, 1) advances a treatment of toxemias that was suggested during the war. Experimentally very encouraging results were encountered, but clinically it is recognized that in profound toxemias the employment of blood-letting followed by transfusion was ineffective owing to the relatively small amount of the total quantity of blood removed and replaced. As experience with this method increased it was recognized that the more complete the replacement of the patient's blood with fresh blood, the greater the effect on the toxemia and the greater chance of the improvement being permanent. The principle of the operation is to withdraw blood from the median basilic vein of the donor or donors into 100-cc glass syringes, each of which contains 10 cc of freshly prepared 3.5 per cent sodium citrate solution. A quantity equal to the total circulation of the individual is thus obtained. In estimating the amount required it is considered that the quantity of blood in any patient's circulation is roughly 35 cc per pound of body weight. The cannula for the transfusion is first introduced and tied in a suitable vein, such as the internal saphenous at the ankle or the median basilic at the elbow, and salt solution is slowly introduced to prevent clotting. The exsanguination cannula is then inserted. In small infants, the superior longitudinal is made use of for exsanguination, but in children in whom the anterior fontanelle is closed the femoral vein provides a suitable substitute. Blood is withdrawn from the patient until signs of exsanguination begin. The amount that can be withdrawn from small children varies from 60 to 160 cc. With the first sign of weakening pulse, one of the 100-cc syringes containing citrated blood from the donors is connected with the cannula and the introduction of fresh blood is begun. After transfusion has been begun, introduction and withdrawal of blood are kept up at the same rate until all the available blood has been transfused. The beneficial effect of this procedure in certain profound toxemias and septicemias has been demonstrated clinically on a great many occasions.

In cases of severe superficial burns, in which the symptoms indicate a possibly fatal result, exsanguination-transfusion has reduced the mortality from 100 to 50 per cent. In erysipelas of the new-born, the mortality has been reduced from nearly 100 per cent to 50 per cent, and in patients from one month to twelve months of age, it has been reduced from 50 to 13 per cent. In acute septic scarlet fever, the method seems to be of decided value in tiding the patient over the period of intense intoxication as well as converting the case into one of the ordinary type. In acute intestinal intoxication the procedure has reduced the mortality from 20 to 25 per cent of the former rate. The results in septicemia are somewhat disappointing. Although there was marked response in some cases, the benefit seemed to be slight and temporary. This was especially the case in staphylococcus infection and in endocarditis.

The Mechanism of Infection and Immunity in Congenital Syphilis.—KOLMER (*Atlan. Med. Jour.*, 1924, **27**, 707) states that in fully 90 to 95 per cent of cases evidences of syphilis will be found in the mothers and the infection is probably a direct one of the children by placental transmissions of Spirocheta pallida. It may be argued that the placenta is well known to be a filter of organisms and that the child in the uterus very commonly escapes infection during septic or other infections of the mother, but the Spirocheta pallida is an exception and by reason of its ability to infect the smallest perivascular lymph spaces is enabled by this biological quality to break through the placental barriers capable of restraining streptococci, pneumococci, tubercle bacilli and the like. Small-pox is another exception that the placental barrier does not stop. In the majority of cases it appears that spirocheta pallida is transmitted to the fetus during the spirochetemic stage of syphilis of the mother. Just prior to and during the clinical secondary stage of syphilis of the mother spirochetemia is most marked, and infection of the child is consequently most likely to occur at this time of the pregnancy, but even during the later years of syphilis, temporary periods of spirochetemia develop with transmission of Spirocheta pallida from old foci to new tissues and organs of the mother and it is possible for the spirocheta to invade the new tissues of pregnancy including the fetus. It is also possible for conception to occur and pregnancy to terminate at full term without infection of the placenta or child during the latent periods of syphilis of the mother, especially after repeated pregnancies have thrown her syphilis into extreme stages of latency. Infection of the child depends on whether or not anything disturbs this latency of the mother, with the production of spirochetemia. If this occurs the child will become infected, but if it does not occur the child will escape. Except for the danger of congenital syphilis, pregnancy could be regarded as a therapeutic measure of value for the mother since it greatly increases her immunity and tends to protect her against the development of old lesions and the production of new ones especially in the tissues of the central nervous system.

Cause and Treatment of Otitis Media.—SMITH (*Am. Jour. Dis. Child.*, 1924, **28**, 1) found in 613 admissions 33.4 per cent of the children had otitis media when they came in or developed it in the hospital. The race and sex of the patient seemed to have no influence of the incidence

of the disease. There was a definite seasonal variation. In February 47.3 per cent of the patients had otitis media. In July only 23.6 per cent were attacked. The most susceptible group was between the ages of three and fifteen months. In this group 50 per cent of the children had otitis media. Patients with pneumonia, dysentery, nasal diphtheria, pertussis and pyelitis developed otitis media in 50 per cent or more of the cases. Those with prematurity, nephritis and the non-infectious diseases showed ear infections in less than 21 per cent. Hemolytic streptococci were isolated from the aural discharge in 56 per cent of the cases cultured. The average duration of the disease was twenty-five and a half days. He found that practically all the Gram-negative bacteria found in the ears of patients suffering from otitis media except B. pyocyaneus are killed by an 0.5 per cent solution of sodium hydroxy-mercuri-benzo-phenone sulphonate. B. pyocyaneus are readily eliminated by treatment with 2 per cent acetic acid or preferably with 0.5 per cent of the sodium solution that contains 2 per cent of acetic acid. All the Gram-positive bacteria found in otitis media are readily killed by gentian violet except streptococci. Neutral acriflavine has been proved to be more potent in the treatment of otitis media associated with streptococci, but even this drug is not entirely satisfactory. Twenty cases of chronic otitis media were cured by local chemotherapy in an average of seven days each. Sixty cases of otitis media were cured in an average of thirteen days each.

Roentgen-ray Studies of Stomach Function.—Rogatz (*Am. Jour. Dis. Child.*, 1924, **27**, 53) undertook his work in order to study the various functions of the infant stomach, about which there was a marked divergence of opinion in the scant literature. Fluoroscopic examinations and roentgenograms of the stomach were made at regular intervals before and after meals, with observations concerning form, size, position, air bubble peristalsis and emptying-time. Three types of feeding were used with each child; milk diet of average caloric value; a concentrated milk; and a gruel or mush of thick consistency. A gruel or cereal made with milk, no matter how thick it was before ingestion, becomes fluid in the stomach under the influence of the saliva and body heat, whereas a food of mashed potato or vegetable mush retains its consistency. The empty stomach is difficult to see with the fluoroscope. The filled stomach is clearly visible without contrast mediums and lies in the upper, left quadrant of the abdomen, close to the diaphragm, extending in a horizontal plane to or just beyond the midline. The stomach shadow on the plate may be defined by an upper, deeply shaded portion due to the air bubble, and a lower, less intensely shaded area which is the stomach contents. The air bubble varies in size, shape and form in all stomachs, with fluid content, but it is distinctly smaller, or often absent, when thick gruels are swallowed. There are two main, constant types of stomach with fluid feedings. Both are horizontal and extend to or just beyond the vertebral column to the right. One shape is that of a pear or a flask lying on its side, with a large circular expanded fundus and a smaller, narrow pyloric area. The other occurs less frequently and is smooth, elliptical or oval in shape. A third form may appear in either of the first two types when thick gruels are ingested. This is a small circular or oval form, about one-third the size of the fluid forms, with little or no air bubble.

DERMATOLOGY AND SYPHILIS

UNDER THE CHARGE OF

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An Experimental Study of the Etiology of Herpes.—MARIANI (*Arch. f. Derm. u. Syph.*, 1924, **147**, 259) publishes with a full bibliography the results of an extended experimental study of various forms of herpes, including simple febrile, progenital, aphthous and zoster types. He regards the various clinical forms of herpes as merely variations on a fundamental reaction process whose clinical differentiation is merely of relative importance. The fundamental fact in the pathogenesis of herpes is an injury to the nervous system, by direct or indirect infection, exogenous or endogenous toxic, or traumatic agents. Existing theories of the mechanism of this action are so complex, indefinite and unsatisfactory as to offer little tangible basis for study. The author frankly states that the same causes, acting through the nervous system may in one case produce simple and in the other zosteriform herpes. Mariani attacks the etiologic problem by inoculation of rabbits with the fluid from unbroken herpetic vesicles, obtained under precautions against contamination and with suitable controls drawn from other bullous or vesicular non-herpetic dermatoses. His conclusions are summarized as follows: Herpes zoster is not autoinoculable and cannot be transferred from person to person in man. Cutaneous inoculation is likewise negative in rabbits and guinea-pigs. Corneal inoculation in guinea-pigs is likewise negative. But in rabbits a form of keratitis may be induced by the vesicle fluid. In febrile or simple herpes, such inoculations on the rabbit's cornea were almost invariably positive, giving rise to a distinctive form of keratitis which did not occur with other vesicle fluids used as controls. The keratitis thus induced in rabbits followed a typical course, regardless of the source of the material, which was obtained from herpes occurring in a wide range of febrile diseases. This herpetic keratitis was inoculable from animal to animal, retaining its clinical and pathologic characteristics but with occasional inexplicable attentuations or accentuations of the virulence of the virus in successive inoculations. Filtered material from herpetic keratitis gave positive inoculations with milder manifestations in fresh animals. Cutaneous and intramuscular inoculations failed uniformly. After intravenous injection of the material, positive results could only be obtained by previously scarifying the cornea. It was observed that herpetic keratitis might develop in the uninoculated eye, and in these cases an infiltrative perineuritic process affecting both eyes by way of the optic nerves and chiasm was recognized. In other animals, both after inoculation from man and from other animals, symptoms in the nervous system constituting apparently a form of encephalitis developed, terminating fatally in many cases in from three to five days. The onset of the encephalitic syndrome was usually on about the tenth day after

the first appearance of the keratitis. Histologically it was possible to demonstrate in these cases, both a meningeal phase, and degenerative changes in the nerve cells. Subdural inoculation of rabbits with filtered or unfiltered brain material from animals with "herpetic" encephalitis, produced encephalitis, and encephalitis could likewise be directly induced by inoculation of filtered or unfiltered material from herpetic keratitis. This was especially true if the source of the herpetic fluid was a rabbit infected from a patient with lethargic encephalitis. Simultaneous inoculation of both rabbit corneæ led to bilateral keratitis. If only one cornea was inoculated the other cornea remained susceptible for about twenty-five days, after which an immunity or resistance to inoculation developed lasting about eighty days. Inoculation with zoster material did not confer any more prolonged immunity than that from ordinary herpes notwithstanding the tradition of prolonged immunity following atracks of zoster in man. No immunity against herpetic keratitis was conferred by other modes of inoculation of the virus in rabbits, nor were any drugs found whose use protected against corneal inoculation of the virus. The existence of a syphilitic keratitis did not protect the involved cornea from inoculation with the herpetic virus. Inoculation of saliva from patients with herpes, and of spinal fluid from a patient with severe meningitis whose febrile herpes produced a sharp herpetic keratitis in rabbits, gave negative results. It was possible to obtain keratitis-producing material from the intracutaneous tissues of herpes carriers, but no inoculation from rabbits to man could be obtained. Progenital herpes of many varieties gave almost invariably positive inoculations on the rabbit cornea, differing in no important particulars from that produced by febrile herpes. A few examples of herpetic keratitis from herpetic aphthous lesions were also obtained. The cultural studies of herpetic material yielded staphylococci, pseudodiphtheroids and a Gram-positive diplococcus. No reactions on the cornea could be obtained from these cultures except in the case of *S. albus*, in which case a purulent ulcerative keratitis differing from the herpetic type developed. In his critical discussion the author concludes that herpes zoster is not an etiologic entity. The infectious character of herpes in general is regarded as presumptively established. The virus has apparently a special affinity for the nervous system and for epidermal tissues, the two factors being inversely related, and one or the other coming to the fore under varying conditions. The virus is regarded as filterable one, capable of producing both herpetic lesions and encephalitis. Many of the clinical manifestations of herpes are due, not to the virus but to subsequent secondary infection with other organisms. The author dwells upon the wide variability in virulence of the virus which in some cases give rise merely to benign herpes and at the other extreme, to grave encephalitic manifestations, and points to the possibility that investigations such as his may have a bearing on the etiology of encephalitis lethargica and molluscum contagiosum.

Skin Resistance to Ultraviolet Light.—MAYER (*Arch. f. Derm. u. Syph.*, 1924, **147**, 238) concludes as the result of an experimental study that increase in pigment is not a necessary factor in the development by the skin of resistance to ultraviolet light. Vitiliginous depigmented

areas under exposure to ultraviolet light undergo the same reduction in susceptibility to turpentine and cantharides as do pigmented areas.

Gold Sol Reaction.—Pick (*Arch. f. Dermat. u. Syph.*, 1923, **144**, 105), in a series of studies of the gold sol reaction in syphilitic spinal fluid states that the changes are highly characteristic for syphilitic fluids. Too much emphasis cannot be placed on the questionable reactions which persist at times after treatment. He observed paretic gold sol curves in staphylococcic meningitis, endothelioma of the dura, and tumor cerebri.

Keratosis Blennorrhagica from Roentgenotherapy.—Oelze (*Arch. f. Dermat. u. Syph.*, 1923, **144**, 1) reports a case of keratosis blennorrhagica apparently provoked by roentgen-ray treatment applied to a gonorrheal joint for the relief of pain. A large group of keratotic lesions appeared at the site which had been subjected to the radiation and other quite characteristic lesions appeared upon the toes. A careful search was made for the gonococcus in the lesions with negative results, a finding in accord with that in the literature at large.

GYNECOLOGY

UNDER THE CHARGE OF

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Results of Radiation on Cancer of the Cervix.—The literature of today is pregnant with articles relative to the use of radium in the treatment of cancer of the uterine cervix. A close scrutiny, however, shows a real scarcity of reports of the results of any large series of cases of cervical cancer treated by radium after the crucial five-year period has passed. Therefore it is particularly interesting to note a report of the cases treated at "Radiumhemmet," Stockholm, which has been written by Heyman (*Jour. Obstet. and Gynec. of the Brit. Emp.*, 1924, **31**, 1) and which deals only with cases of carcinoma of the cervix. "Radiumhemmet" is a hospital founded by the Cancer Society of Sweden and partly supported by the Government, which was especially established for the radiological treatment of gynecological cases. Surgical treatment is only employed as an adjuvant to the radiological treatment. In cases of carcinoma of the uterus radiological treatment only is practised. The patients are referred for treatment to "Radiumhemmet" almost exclusively by surgeons or gynecologists, mostly from hospitals and gynecological clinics. As a rule, only three applications of radium are made. The second application is made one week after the first and the third application three weeks after the second. If possible, radium

is applied at each treatment both in the vagina and in the uterus, the length of time of each application being twenty-two hours, using from 33.7 to 40.1 mg. in the uterus each time, making a total dosage of about 2220 to 2640 mc. hours. In the vagina 70 mg. is used three times, making a total dosage of about 4500 mc. hours. The radium is always filtered through 3 to 4 mm. of lead. During the last three years a more concentrated treatment has been tried, the number of applications being reduced to two, thirty-two and twenty-four hours respectively. In such cases the total vaginal dose has been limited to 4000 mc. hours. All operative interference at the commencement of the treatment, such as cauterization or excochleation, is absolutely contraindicated and the treatment is never repeated within the first six months. If, six months after the three applications already mentioned, the growth has not disappeared or if there is a recurrence, the treatment may be repeated, though *preferably* not until a year after the first treatment and only one application is then made. Clinically healed patients, as well as patients with a suspected "reactive" inflammation, are not treated again until a recurrence has been definitely proved. If there is a local recurrence and the growth is operable, hysterectomy is performed. If there are extensive glandular metastases roentgen irradiation is used in conjunction with the radium treatment. It is also used if severe pains persist after the radium treatment and if there is a recurrence in the parametria. This report covers the period of eight years from 1914 to 1921, during which time 505 cases of cancer of the cervix were primarily treated. From 1914 to 1918 the inoperable and borderline cases constituted 91.2 per cent of the series, but from 1919 to 1921 these cases constituted only 68.4 per cent. One-third of the patients were under forty-six years of age; 19.1 per cent were forty years of age or under. In the statistics which follow, all the patients who have died have been counted as dying from cancer.

Operable or Borderline Cases:

1914–1918	40.5 per cent free from symptoms after 5 years.
1919	47.3 per cent free from symptoms after 4 years.
1920	60.0 per cent free from symptoms after 3 years.
1921	58.3 per cent free from symptoms after 2 years.

Inoperable Cases.—1914–1918. 16.6 per cent free from symptoms after five years. Of the remainder 20 to 25 per cent, varying with the year, were free from symptoms after three years. Heyman has observed that if local recurrence occurs, as a rule it does so within one year, but glandular recurrence and metastases may supervene after years of apparently good health. Pain, anemia and fever nearly always indicate the presence of cancer in the pelvis. The complications due to radium treatment are chiefly rectal, which appear as a rule, six months after the treatment, and are due to overdosage and include tenesmus and hemorrhage. Since 1915 he has not had a case of fistula, while 5 patients died of diffuse peritonitis and sepsis as the result of the treatment and one from pulmonary embolism. The primary mortality in this series is 1.19 per cent.

Nature of Uterine Secretion.—In his recent contribution to the literature, Kross (*Am. Jour. Obstet. and Gynec.*, 1924, **7**, 310) recalls his previous experimental work which we have already quoted, showing that the uterine secretion in the rat was able to increase, to a marked

degree, the coagulation period of blood taken from rats, guinea-pigs, and man. In addition to this property, the mixture of uterine secretion and blood after its coagulation, became fluid, as a result of a fibrinolytic ferment present in the uterine secretion. The findings of the above experimental investigation of uterine secretion in the rat taken in conjunction with the phenomenon of menstruation, seemed to point to the solution of the problem of the incoagulability of menstrual blood. It is fair to assume that the menstrual blood is mixed with the uterine secretion as it passes through the endometrium, and that the uterine secretion interferes with coagulation by delaying it sufficiently to allow the fibrinolytic ferment to dissolve any of the small clots that may form. In order to prove that there exists in the human being a uterine secretion similar to that found in the rat, Kross employed the hematocolpos fluid obtained from one of the patients in the gynecological ward of the Mt. Sinai Hospital. The patient, aged sixteen years, presented the typical picture of an imperforate bulging hymen with a history of amenorrhea with periodical monthly attacks of pain in the lower abdomen for a year. The hymen was incised under aseptic precautions and the thick tarry accumulation of old menstrual blood was carefully saved. About 10 cc of this fluid were mixed with an equal quantity of blood taken from the median veins of other patients. A control specimen of unmixed blood was also taken in every instance. The hematocolpos fluid was in this way tested with the blood of seven other individuals and in every instance there was a marked increase in the coagulation period. The nature of the clot formed by the mixture of the two bloods differed very distinctly from that formed by the control blood. In the former, the blood clot was much softer and much more jelly-like. The tubes containing the mixed bloods and those containing the control bloods were then placed in the incubator. After a period of time varying from one-half to four hours, it was noted that the clot formed in the mixture became softer, and finally in four instances became completely fluidified. In the other instances, the fluidification was almost complete and the residual clot very small and extremely soft. The clots in the control tubes on the contrary, became progressively harder and showed absolutely no tendency towards fluidification. From these results, Kross believes that it is fair to state that the hematocolpos fluid is thoroughly mixed with uterine secretions that contains a fibrinolytic ferment similar to that present in the rat and that its fluid nature is due to the action of this ferment. Similarly it can be stated that in the normal individual, the menstrual blood is fluid and that it does not clot subsequent to its escape from the uterus and vagina, as a result of the activity of this ferment. Where the menstrual fluid is composed of more or less clotted blood in an individual whose internal genitalia are not the seat of an abnormal anatomical change, it seems proper to conclude that in that case there is a deficiency of this fibrinolytic or thrombolytic ferment.

A Modified Gilliam Operation.—The operation which LEICESTER (*Jour. Obstet. and Gynec. of the Brit. Emp.*, 1924, **31**, 68) describes as an improvement on the classical Gilliam procedure is performed by opening the abdomen through a transverse incision. After incising the skin and before dividing the aponeurosis, the lower flap is carefully dissected from the aponeurosis in a downward direction until both the

external abdominal rings are exposed and clearly defined. After the peritoneal cavity is opened, the uterus is pulled up, and a silkworm gut suture is passed around each round ligament and tied not less than three-quarters of an inch from its attachment to the uterus. A Lucas nephrectomy needle is then passed into each external abdominal ring, along the inguinal canal and then inward parallel to the round ligament, under the peritoneum of the broad ligament, until the site of the ligature is reached. During this process the round ligament is kept taut by an assistant pulling on the ligature. The needle is then made to emerge through a nick made with a scalpel through the peritoneum, threaded with the two ends of the silkworm-gut ligature and withdrawn. The peritoneum and aponeurosis are then closed with continuous catgut sutures. The silkworm gut ligatures on the round ligaments are now pulled on until a short loop of the round ligament presents at the external abdominal ring, needles are threaded on each end of the ligatures and the loop of ligament on either side is sutured to the pillars of the ring so that when tied the pillars are approximated at the upper part of the ring, which is thus partially closed. The skin is then closed in the usual manner. Leicester has performed the operation in 20 cases with no unpleasant results but as yet has not had the opportunity of determining how it will stand the test of pregnancy.

Mercurochrome Ointment in Vaginitis.—The treatment of vulvovaginitis in children is certainly not standardized and perhaps it will be a long time before the profession will come to any agreement on this subject. A few years ago we called attention to the recommendation of Gellhorn that a 1 per cent silver nitrate ointment be used in these cases because he stated that he was getting superior results by the use of the preparation. Dorne and Stein (*Ill. Med. Jour.*, 1924, **45**, 219), who have been working on this problem for some time, have substituted a 1 per cent mercurochrome ointment for the silver nitrate, because it is less irritating, less astringent, and equally efficient as a germicide. The ointment is injected into the vagina by means of an ordinary irrigating glass syringe having a slender nozzle, to which a piece of soft rubber tubing 3 inches long and $\frac{1}{4}$ inch in diameter is attached. This tubing is introduced into the vagina and slowly pushed inward along the entire length of the vagina. The vagina is then slowly filled to capacity with the mercurochrome ointment, the excess of ointment being allowed to ooze back through the hymeneal opening, covering and protecting the irritated vulva. The tubing is changed for each patient and is sterilized by boiling. These treatments are given daily and no irrigations or other treatments are allowed, but a daily tub bath is insisted upon. The mothers are urged to change the children's underclothing frequently. The method is so simple that a large number of children can be treated in a short time and is painless so that the children coöperate readily. Since the cultural results were of no material assistance and in some cases failed to corroborate the smear reports, these investigators have ceased to make cultures and rely entirely upon smears in noting the progress of the case. Smears are taken at the beginning of treatment and are repeated every two weeks after a day of rest from treatment. When negative reports are obtained the smears are repeated at weekly intervals until three successive negative smears are obtained. Treatment is then suspended and a smear taken two weeks later and if

negative, repeated finally in three or four weeks to determine cure. Further observation is continued for a period equal to the time of the active treatment before the patient is discharged as cured. Furthermore, the cases are followed up for the next year to determine the permanency of the cure and to detect recurrence. As a result of their experience, Dorne and Stein state that vulvovaginitis in children can be cured by daily injections of 1 per cent mercurochrome ointment into the vagina. In gonorrheal cases they obtained a cure by this method in an average of 9.7 weeks, while in the non-gonorrheal cases cure was obtained in five weeks. In 20 cases which they were able to follow, there were no recurrences in the year following the treatment and therefore they urge the adoption of the method because of its many advantages.

Treatment of Benign Uterine Tumors.—In the Cleveland Clinic, CRILE (*Ill. Med. Jour.*, 1924, **45**, 177) concludes with us that near, during or after the menopause, intramural fibroids of moderate size or fibrosis associated with hemorrhage should be treated by radium or radium plus deep roentgen-ray therapy. On the other hand, in the childbearing period he believes that operation should be advised because the mortality is less than 1 per cent (in his clinic) with permanent relief in nearly 100 per cent. Furthermore surgery assures the preservation of 100 per cent ovarian balance and preserves to a surprising degree the childbearing function. There is one type of operation which formerly baffled the surgeons but which Crile believes he has conquered, namely, the removal of a fibroid tumor from a pregnant uterus in which the growth is so situated that the obstetrician sees clearly that normal delivery cannot be made and that a premature abortion will destroy the fetus and to some extent imperil the mother. He has found in his experience that in cases where miscarriage attended operation, it did not occur during nor immediately after the operation, but usually twenty-four or more hours later—the miscarriage being preceded by a period of labor pains. In considering the large numbers of physical injuries unattended by fear that a woman may sustain without miscarriage, and on the other hand the frequency with which a miscarriage occurs as the result of a strong emotional shock, it occurred to Crile that the removal of the emotional factor might obviate the danger of miscarriage. He therefore adopted the following plan of treatment: (1) That the patient be kept in ignorance of the day appointed for operation; (2) that a physiological dose of morphin be given an hour before the administration of the anesthetic; (3) that the patient be given light nitrous-oxid-oxygen anesthesia in bed and be taken under this anesthesia to the operating-room; (4) that during the operation the entire field—abdominal and uterine—be blocked with novocain; (5) that during operation handling of tissues be reduced to a minimum; (6) that the patient be returned to her bed under anesthesia of light nitrous-oxid-oxygen; (7) that the patient be kept under morphin for forty-eight hours after operation, much water being given during this period; (8) that at the end of forty-eight hours the morphin be diminished, unless the slightest rhythymic pain occurs, in which case morphin should again be increased. By this plan of management he has removed myomata as large as the fetus and has even exposed the placenta without a single postoperative contraction pain. Another interesting group

of cases is the type of woman who is at or past the menopause, in whom examination reveals a normal vagina and cervix, no fibroid and but slight thickening of the uterine wall, the only sign of trouble being a slowly increasing amount of discharge which may or may not be stained with blood. Such patients as these belong in the precancer class, in fact, 5 or 10 per cent show cancer. Crile believes that a hysterectomy is indicated in such cases whether or not cancer is found, since if there is no cancer today, do we know that there will not be a cancer another day? Moreover, these senile changes are usually not cleared up by curettage. In brief, the patient secures safety against the future and relief from local trouble at the expense of but a trivial discomfort and a negligible risk.

Error to be Avoided in Ureteral Catheterization.—Some years ago it was decided to introduce as a routine procedure preliminary to roentgen-ray examination, shadowgraph catheters into the ureters rather than ordinary catheters when trying to determine the exact position of shadows suspicious of being in the ureter. In doing routine work, when a catheter is introduced into the ureter and is readily introduced some 25 to 35 cm., no evidence of obstruction or retention being encountered, one is naturally inclined to arrive at the conclusion that the catheter has reached the upper limit of the ureter and is resting somewhere near the kidney pelvis. Recently however, BEER (*Jour. Urol.*, 1924, **11**, 425) had two such cases where the catheter entered readily and there was no suggestion that the catheter had turned on itself, but a roentgen-ray picture with the catheters in the ureter showed how faulty the inference was since in both instances the catheter twisted on itself a number of times and was lying in this twisted condition in the lower ureter, although the examiner might readily have inferred that it had readily passed to the kidney. It is apparent therefore, that unless one has a roentgen-ray control, one cannot infer, no matter how easily the catheters enter some 30 to 35 cm. up the ureter, that they are in fact in the kidney pelvis.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF
OSKAR KLOTZ, M.D., C.M.,
PROFESSOR OF PATHOLOGY, UNIVERSITY OF TORONTO; TORONTO, CANADA,
AND
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A Bacteriologic Study of Extirpated Tonsils.—Because of the important role played by the tonsils in focal infections, it is of interest to place on record the bacteriological findings in cultures made from the crypts of extirpated tonsils. JULIANELLE (*Jour. Lab. and Clin. Med.*, 1924, **9**, 699) studied at the Philadelphia General Hospital a series of hypertrophied or septic tonsils from 147 patients, by culturing material removed from the depths of the crypts on the surface of beef-infusion blood agar. Further identification of the bacteria revealed that hemo-

lytic stretptococci were encountered in 90.4 per cent; staphylococci in 62.5; Streptococci viridans in 31.2; M. catarrhalis in 19.7; B. influenzæ in 17; pneumococcus in 8.8; B. mucosis in 5.4; B. diphtheriæ in 4 and nonhemolytic streptococci in 1.3 per cent. In 8 instances pure cultures were obtained—hemolytic streptococci in 7 and Streptococci viridans in 1. The author indicates that the percentage incidence of the various bacteria in his work was somewhat lower than that of Pilot and his co-workers (*Jour. Inf. Dis.*, 1921, **29**, pp. 47, 51, 55, 59 and 62), but was in fair agreement with that of Caylor and Dick (*Jour. Am. Med. Assn.*, 1922, **78**, 570).

The Myocardial Lesions of Diphtheria.—After a most comprehensive résumé of the literature, WARTHIN (*Jour. Infec. Dis.*, 1924, **35**, 32) found that the development of the theories of cardiac pathology in diphtheria presented an evolution closely paralleling that of the general theory and science of medicine during this period (1860–1924). The phases of this evolution, he classed as follows: "(1) Cardiac paralysis; (2) cardiac thrombosis; (3) infectious endocarditis; (4) endarteritis of cardiac vessels; (5) infectious parenchymatous myocarditis; (6) infectious interstitial myocarditis; (7) injury to cardiac nerves and ganglion, vagus, abdominal sympathetic and vasomotor system, resulting in cardiac paralysis; (8) toxic myocarditis; (9) special affinity of diphtheria toxin for the impulse-conducting system of heart (bundle of His)." In the attempt to clarify some of the questions and to give a more definite entity to the cardiac pathology of diphtheria, the autopsy material from 16 cases was studied grossly and microscopically. It was found that "the essential lesion of the heart in diphtheria was a toxic parenchymatous hyaline degeneration or necrosis, associated frequently with fatty degenerative infiltration and less frequently with cloudy swelling or simple necrosis." If the patient survived a sufficient length of time a reparative inflammatory process (myocarditis), accompanied by muscle regeneration, followed the degenerative lesions. Either a complete regeneration or a fibrosis could result. Both the conducting and contractile mechanisms of the heart were damaged by the diphtheria toxin, there being no particular affinity for either apparatus. The author states that "the histologic picture in any given case will depend on the duration and stage of the infection, upon the degree of toxin injury to the muscle, the associated nutritional conditions, and the degree of muscle regeneration and accompanying fibrosis." It was of interest that 9 of the 16 cases presented well-marked features of the thymicolymphatic constitution, "again an emphasis of the liability of this constitution to death from acute infections."

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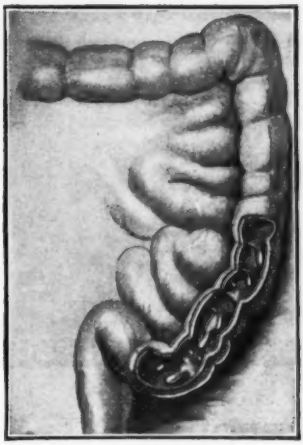

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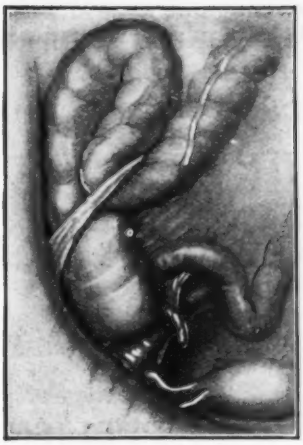

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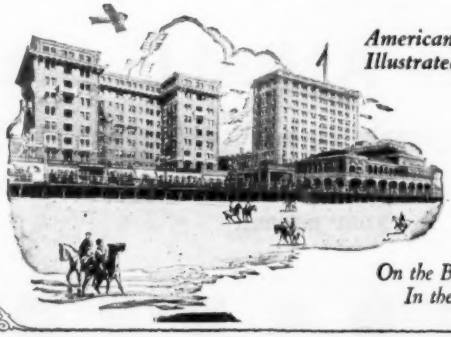

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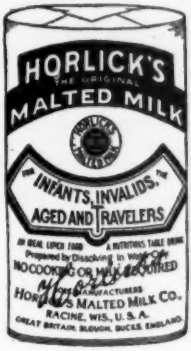

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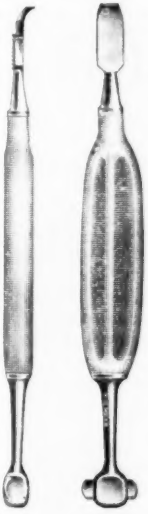

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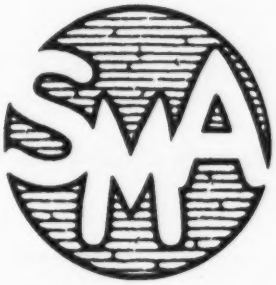

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